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RESEARCH ARTICLE

SURVIVAL OF PATIENTS USING ANTIRETROVIRAL THERAPY BY PASS STIGMA, SOUTH ETHIOPIA

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ABSTRACT

Human Immunodeficiency Virus| Acquired Immune Deficiency Syndrome (HIV|AIDS) has become the common deadly chronic disease. Provision of antiretroviral drugs is believed in reducing the effect of stigma and social discrimination. Previous studies verified the association between accesses of ART on stigma reduction. In this study, the urban data results confirmed with the previous study results. However, the rural data do not reflect the access of ART reduces the stigma of patients on ART. Most of patients in rural hospitals give up continuing on ART due to stigmatization. As a result the survival probabilities of rural patients on ART in Gidole (rural hospital) become 0.0997 in 104th survival month from 0.9956 in 17th survival month. For the same survival months, the survival probabilities of patients on ART in Arba Minch (urban hospital) become 0.5924 from 0.9936. To improve the survival probability of patient, we should improve CD4 count. It is the main determinant factor in patient survival modeling.

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INTRODUCTION

Human Immunodeficiency Virus| Acquired Immunodeficiency Syndrome (HIV|AIDS) has become the most deadly epidemic disease in history. Ethiopia being one of the highly affected countries, HIV|AIDS is the leading cause of morbidity and mortality. People living with HIV|AIDS have been stigmatized since the beginning of the epidemic leading to severe social consequences related to their rights, health care services, freedom, self-identity and social interactions. Factors that contributed to stigma include the fact that HIV|AIDS is considered as an incurable disease and people are scared of contracting HIV (Brown *et al*., 2003). Religious or moral beliefs lead some people to believe that HIV|AIDS is the results of moral fault (sin) which deserves to be punished. Stigma is of utmost concern because as it is both the cause and effect of secrecy and denial, which are major catalysts for fueling HIV pandemic. In some places although the advent of free and accessible ART has offered hope and encouraged people to go for testing, stigma remains a barrier to testing. Provision of antiretroviral drugs is believed to contribute in lessening the effect of stigma and discrimination in those who are enrolled in care and treatment. Many people living with HIV|AIDS have a better quality life as the result of increasing availability of ART.

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There was a statistically significant association between duration of ART and favorable effect of access to ART on stigma reduction (Theodros Solomon, 2008). ART drugs have not only improved the life of people living with HIV|AIDS in terms of delaying disease progression and improving quality of life but also seem to have an effect on stigma (Ernosto *et al*., 2006). Antiretroviral has the capacity to transform HIV infection from an incurable "death sentence" into a treatable "chronic illness" reducing the stigma of the disease and stimulating people's willingness to be tested and disclose their sero-status (Ernosto *et al*., 2006). It has been documented that access to highly active ART was a powerful mechanism to reduce HIV related stigma (Kloos *et al*., 2007).

Ethiopia is one of countries most heavily affected by the epidemic. In response, the government of Ethiopia has taken measures to reduce the risk of transmission of HIV and mitigate the impact of the HIV epidemic on society. Several policies are in place to support the implementation and scaling up the national response, including the National HIV|AIDS Policy, the National Strategic Framework on the Prevention and Control of HIV|AIDS, and the Supply and Use of Anti-Retroviral Drugs Policy. As part of implementing the ART rollout, the MoH (minster of health) issued regional targets and antiretroviral drug quotas for each region based on the estimated number of people living with HIV|AIDS eligible for ART and geographical and health services parameters. It proposed that catchment areas of individual health facilities be mapped in an effort to facilitate the equitable distribution of ART (MoH, 2005). An earlier study on the size of catchment areas for polyclinic outpatients and inpatients in different parts of the country showed that they range from *wereda* (district) sized areas for health centers to entire regions for well established hospitals. Data on patients treated in each hospital and health center can be accessed from the ART clinics of catchment area. The requirements, criteria and procedures for enrollment for free ART include the following: HIV test results, personal and behavioral eligibility as it has an effect on adherence to treatment, some laboratory investigations, including hematology, CD4 counts and blood chemistry to determine the eligibility for and safety of ART. Shortly after the launching of the free ART scheme, all patients were requested to bring a poverty certificate for free ART from their *kebele* administration office which also verified patients' place of residence. But later on this proved to be stigmatizing and was a barrier for patients to get treatment at the health facilities. Therefore, this requirement was abolished and currently ART is free throughout the country for all patients who need the treatment and are medically eligible for the treatment. Voluntary counseling and testing (VCT) constitutes an integral part of the enrollment process, as described in the Ministry of Health Guidelines for Use of Antiretroviral Drugs in Ethiopia to promote adherence, confidentiality, and de-stigmatization (MoH, 2003).

METHODS

Data

The patients' data were analyzed here are categorized into three initial stages or phases of the HIV/AIDS treatment process:1) enrollment for HIV/AIDS care, 2) starting on ART and 3) continuing treatment and currently on ART. The patients' data were collected from health institutions under study catchment areas, Ethiopian Rift Valley, South Ethiopia. Each and every important aspects of ART users' information has been recorded in those institutions. Those institutions are general zonal hospitals, health centers, and ART clinics.

Statistical Techniques

In survival studies, the response variable of interest is the amount of time from an initial observation until the occurrence of a subsequent event. Examples include the time from birth until death, the time from transplant surgery until the new organ fails, and the time from the start of maintenance therapy for a patient whose cancer has gone into remission until the relapse of disease. This time interval between a starting point and subsequent event, often called a failure, is known as the **survival time.** Although the measurements of survival times are continuous, their distributions are rarely normal; instead, they tend to be skewed to the right. The analysis of this type of data generally focuses on estimating the probability that an individual will survive for a given length of time.

One common circumstance in working with survival data is that not all the individuals in a sample are observed until their respective times of failure. If the time interval between the starting point and subsequent failure can be quit long, the data may be analyzed before this second event of interest has occurred in all patients. Other patients who either move away before the study is complete or refuse to participate any longer are called to be ***lost to follow-up***. The incomplete observation of a time to failure is known as ***censoring***; the presence of censored observations distinguishes the analysis of survival data from other types of analyses.

A distribution of survival times can be characterized by a **survival function**, represented by $S(t)$. Survival function is defined as the probability that an individual survives beyond time *t*, equivalently, for a given time *t*, $S(t)$ specifies the proportion of individuals who have not yet failed. If T is a continuous random variable representing survival time, then

$$S(t) = P(T > t) \quad (1)$$

The graph of $S(t)$ versus time *t* is called **survival curve.** A survival curve can be approximated by plotting the survival function $\hat{S}(t)$ generated using the life table method versus the point representing the start of each interval, and then connecting the points with straight lines. The classical method of estimating a survival curve is known as the *life table method.* This technique parallels the study of life tables in demography. Ideally, we would prefer to work with a *longitudinal life table,* which tracks an actual cohort of individuals over their entire lifetimes. This method is not practical for large population studies; it would involve following a sizable group. However, it is often used in smaller clinical studies in which patients are enrolled sequentially and followed for shorter periods of time.
When we use the life table method, the estimated survival function $\hat{S}(t)$ changes only during the time intervals in which at least one death occurs. The product-limit method of estimating a survival function, also called **Kaplan-Meier method**, is a nonparametric technique that uses the exact survival time for each individual in a sample instead of grouping the times into intervals.

When the product-limit method is used, $\hat{S}(t)$ is assumed to remain the same over the time periods between deaths; it changes precisely when a subject fails. Using LIFETEST statement in SAS, the product-limit survival estimates and its curve have been produced.

The Kaplan–Meier (1958) estimator is the nonparametric maximum likelihood estimate of $S(t)$. It is a product of the form

$$\hat{S}(t) = \prod_{t_i \leq t} \frac{n_i - d_i}{n_i} \quad (2)$$

When there is no censoring, n_i is just the number of survivors just prior to time t_i. With censoring, n_i is the number of survivors less the number of losses (censored cases). It is only those surviving cases that are still being observed (have not yet been censored) that are "at risk" of (observed) death. d_i is the number of deaths in given time interval *i.* Let T be the random variable that measures the time of failure and let $F(t)$ be its cumulative distribution function. Note that

$$S(t) = P[T > t] = 1 \quad P[T < t] = 1 \quad F(t) \quad (3)$$

Consequently, the right-continuous definition of $\hat{S}(t)$ may be preferred in order to make the estimate compatible with a right-continuous estimate of $F(t)$. The Kaplan–Meier estimator is a statistic, and several estimators are used to approximate its variance. One of the most common such estimator is Greenwood's formula:

$$\hat{V}\left(\hat{S}(t)\right) = \hat{S}(t)^2 \sum_{t_i<t} \frac{d_i}{n_i(n_i-d_i)} \quad (4)$$

In some cases, we may wish to compare different Kaplan–Meier curves.

RESULTS AND DISCUSSION

There are advances in today the availability, accessibility and utilization of HIV|AIDS prevention, care, and treatment services. Fortunately, both government and non-government organizations are working hard to restrain the epidemic and the achievements of these years are encouraging in Ethiopia. However, it can be observed less attention was given for researches dealing with survival trend of patients in different demographic and geographic conditions of ART users. The patients' survival data from different hospitals in Ethiopian refit valley towns has been collected and analyzed. Here, HIV/ADIS patients' survival data of two geographically adjacent hospitals (Gidole and Arba Minch) have been compared. The tables blow show survival probabilities of patients on ART.

Average survival probability of patient in Gidole hospital and Arba Minch hospital, at 17th survival month on ART, were 0.9956 and 0.9936 respectively. These figures show that the same statistical result of survival of patients when they started ART in two hospitals. However, the survival probabilities of patients differ in two hospitals for further survival of patients on ART. At 104th month of survival of patient on ART, the probability of survival in Gidole hospital was rapidly reduced to 0.0997, but in Arba Minch hospital was slowly reduced to 0.5924. This discrepancy raised due to geographical and living style differences of patients around two hospitals. Arba Minch hospital is an urban and equipped better skilled men power than Gidole hospital which is a rural one. The awareness of the patients in urban hospital is better than that of rural patients in health care activities; this may advance good survival status of urban patients on ART than rural. The feeding style and access of balanced diet is considerable factor to raise the survival difference between urban and rural patients'. The stigmatization behavior of rural population create barrier for patients to go testing and having treatment regarding ART.

Modeling the impact of patient age, weight and CD4 count on survival months of patients on ART was other focus area of this study. The results showed that CD4 count significantly determine the survival of months of patients on ART. The patient weight statistically does not provide relevant result. It showed in some hospitals positive relation with survival months of patients on ART; however, it showed negative relationship with survival months of other hospitals. This controversy implies it is not relevant variable to determine survival months of patients on ART.

Table 1. The survival distribution of HIV/ADIS patients on ART in two hospitals (Gidole and Arba Minch)

Time(month)	Survival	Failure	Standard Error	Number Failed	Number Left
Gidole Hospital					
0.000	1.0000	0	0	0	234
17.000	**0.9956**	0.00437	0.00436	1	228
29.000	0.9540	0.0460	0.0142	10	201
40.000	0.9247	0.0753	0.0181	16	183
49.000	0.8409	0.1591	0.0265	31	141
60.000	0.7218	0.2782	0.0346	49	101
70.000	0.6531	0.3469	0.0381	58	79
79.000	0.5534	0.4466	0.0426	69	55
90.000	0.3988	0.6012	0.0513	80	21
102.000	0.1496	0.8504	0.0620	89	3
104.000	**0.0997**	0.9003	0.0580	90	2
Arba Minch Hospital					
0.000	1.0000	0	0	0	1719
17.000	**0.9936**	0.00640	0.00192	11	1708
29.000	0.9159	0.0841	0.00681	140	1456
40.000	0.8673	0.1327	0.00848	214	1255
50.000	0.8234	0.1766	0.00982	272	1007
60.000	0.7792	0.2208	0.0111	321	787
70.000	0.7387	0.2613	0.0125	357	589
80.000	0.6950	0.3050	0.0143	385	341
90.000	0.6541	0.3459	0.0176	398	137
99.000	0.6121	0.3879	0.0235	404	78
104.000	**0.5924**	0.4076	0.0265	406	60
111.000	0.5369	0.4631	0.0414	409	18

Table 2. Analysis of Variance

Dependent Variable: survival month

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Gidol Hospital					
Current weight	1	**-0.01305**	0.11847	-0.11	0.9124
currentCD4	1	0.02617	0.00582	4.49	<.0001
age	1	-0.15835	0.11594	-1.37	0.1732
baseCD4	1	0.02070	0.00547	3.79	0.0002
Arba Minch Hospital					
Current weight	1	**0.02683**	0.12182	0.22	0.8259
currentCD4	1	0.02667	0.00594	4.49	<.0001
age	1	-0.18096	0.12909	-1.40	0.1622
baseCD4	1	0.01900	0.00554	3.43	0.0007

Also the Kaplan-Meier survival curves show the trend of two distributions. For the survival months less than 50, the survival curve of patient, in Gidole hospital, take higher position than Arba Minch hospital; however it take the reverse when the patient survive beyond 50 months on ART. From two curves we observe that survival of patients' on ART in Gidole hospital shows spit slope indicating high mortality but survival of patients' in Arba Minch hospital shows plat slope with moderate mortality rate relative to Gidole hospital.

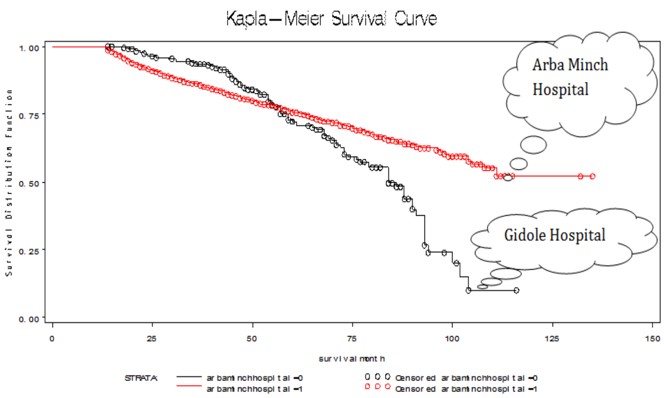

Figure 1. Kaplan-Meier survival curves of two hospitals, Gidole (red) and Arba Minch (black)

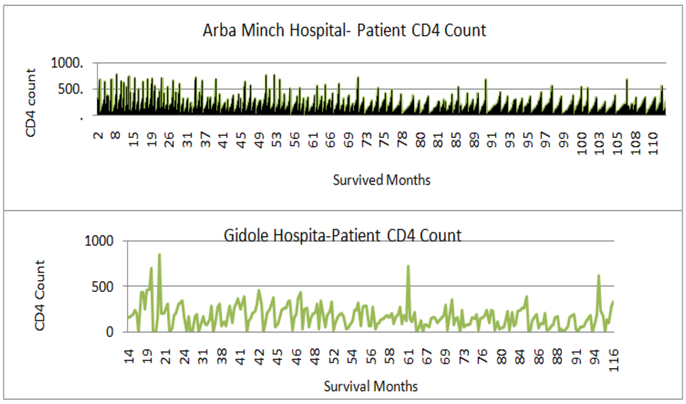

Figure 2. Distribution of CD4 counts

CD4 count of the patient decrease leads to decrease the survival of the patient on ART. Thus improving the CD4 count improves patient's survival on ART. On average the CD4 count of patients in Arba Minch hospital was higher that the Gidole hospital. It contributed higher survival of patients in Arba Minch. The CD4 count distributions of two hospitals in this study are depicted in charts.

Conclusion

Provision of antiretroviral drugs is believed to contribute in lessening the effect of stigma and discrimination in those who are enrolled in care and treatment. Also it expected to elongate patients' survival. These facts were also supported by this study in urban hospital. There is an indication of survival in the patients on ART. However, rural patients on ART do not free from stigmatization and discrimination. Stigmatization and discrimination behavior of rural population make barrier to patients to go to testing and counseling. Most of rural population in study area characterizes the disease as a result of sin and social moral failure of the patient. As a result, patients even on ART stigmatized and cease themselves from drug consumption. This is one of the reasons why survival of patients on ART in rural hospital was shorter than the urban. Thus the mortality rate of rural patients on ART has higher than urban patients on ART. This is due to geographical, awareness, feeding system and health care differences between urban and rural. The CD4 count improvement determines longer survival of patients on ART. Physicians should give high attention for factors that improve CD4 counts to increase proportion of individuals who have not yet failed. The government and non-government organizations should be give focus and fill these awareness gaps of rural communities to reduce and limit stigmatization and discrimination over patients on ART to extend the survival months of patients.

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