

Modelling the Status of Patients Undergoing Antiretroviral Therapy Programme in Kebbi State

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Abstract

The paper modeled the status of HIV/AIDS patients undergoing antiretroviral therapy (ART) programme at Sir Yahaya Memorial Hospital Birnin Kebbi, Kebbi State. This is done with a view to determine the future trend of the 3 categories of patients under study as well as to determine whether the current status of patients is dependent on sex and age group of the patients. Trend analysis of time series data and chi-square test of independence were employed on the weekly data collected from Sir Yahaya Memorial Hospital Birnin Kebbi, a Premier Hospital in Kebbi state North western Nigeria for 58 consecutive weeks i.e.5/12/2017-8/12/019. Three functional linear models one each for defaulted patients, dead patients and patients in care were fitted to the collected data and forecast were made on the basis of these models. Results obtained revealed a weekly decrease in the number of default patients which will likely be 0 by the 3rd week of January, 2019. However, an increase was observed in the number of dead and in care patients for the next 14 weeks which implies that the two are likely going to be on the increase though more pronounced in case of in care patients if mitigating measures are not put in place. It was also observed that the current status of patients undergoing antiretroviral therapy (ART) programme at the hospital is independent of their sex and age group. It is recommended that emphasis on good contact tracking methods be maintained by increasing financial resources to serve as an incentive for contact tracking team. This will enable members of the team to identify those who lost follow-up in order to counsel them on drugs adherence, as failure to adhere to treatment will affect the efficiency of the treatment, moreover, information about some patients that died can be traced through contact tracking services.

Keywords: ART, HIV/AIDS, Modelling, Trend Analysis, In-care, Default patients

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Background to the Study

The Acquired Immune Deficiency syndrome (AIDS) pandemic is currently the world's deadliest war that has killed over 35 million people since it was first recognized in 1981, making it one of the most destructive epidemics in recorded history. Despite recent, improved access to antiretroviral therapy (ART) and care programs in many parts of the world, the AIDS epidemic claimed 3.1 million lives in 2015, more than half a million (570,000) were children (WHO/UNAIDS, 2017).

Today, over 36.9 million people are living with Human Immune Virus (HIV) worldwide. Of these, over 30.8 million are adults, 15.8 million are women and 1.8 million are children under 15 years. People who were newly infected with HIV in 2017 alone are 1.8 million. A total of 940,000 deaths due to AIDS were recorded in 2017, of which 330,000 were children below 15 years (WHO/UNAIDS, 2017).

A little more than one-tenth of the world's population lives in sub-Saharan Africa, which remains hardest hit and is home to 25.8 million people living with HIV, almost one million more than in 2013. Seventy percent of people infected with HIV live in sub-Saharan Africa. In 2015 alone, there were 4.9 million new infections, of who 700,000 were children (WHO/UNAIDS, 2016) the adult prevalence of HIV in sub-Saharan Africa is 7.2 % compared with the next highest region – the Caribbean at 1.6%.

Nigeria, the most populous African nation which has a population of over 140 million people (Nigeria 2006 Census), has witnessed rise and fall in the figures with regard to the number of people living with HIV/AIDS in the country. It is obvious that the disease has maintained an inconsistent upsurge in the last two decades. The prevalence rate has continually been on the increase from 1.8 percent in 1992, 3.8 percent in 1994, 4.5 percent in 1996, 5.4 percent in 1999; 5.8 percent in 2001 (FMOH, 2011), with recent decline to 5.0 percent in 2013. Nationally, about 4.4% [4.2%–4.6%] of women attending antenatal clinics were found to be infected with HIV in 2005, but prevalence in pregnant women exceeded 5% in almost a dozen states, while the incidence has lowered to 4.0 percent in 2006. Even with this prevalence rate, only India and South Africa have more people infected with HIV than does Nigeria, where an estimated 2.9 million [1.7 million–4.2 million] people were living with the virus in 2005 (UNAIDS, 2006). Approximately 210,000 adults were newly infected with HIV in 2017. When the improved assumptions used to obtain current estimates of HIV prevalence among pregnant women are applied to previous rounds of sentinel surveillance, the overall trend in HIV infection levels among pregnant women in Nigeria appears to be stable. The epidemic shows considerable variation, with state-wide prevalence ranging from as high as 10% in Benue (in the North Central zone) and 8% in Akwa Ibom (South South zone) to under 2% in Ekiti, Oyo (both in the South West zone), and in Jigawa (North West zone). In some states, HIV prevalence among pregnant women is higher in rural than in urban areas, while in others the reverse is being found (Federal Ministry of Health Nigeria, 2011).

Statement of the Problem

When patients drop out of ART programs they get sicker with severe opportunistic infections that are more expensive to treat and difficult to manage; or they die. Those who stop taking antiretroviral therapy due to various reasons that are not yet clearly elucidated; also stand the risk of developing resistance to the relatively cheaper and convenient first-line regimens. Treatment discontinuation raises some of the same concerns about drug resistance as adherence does and even worse, negates much of the benefit sought by those in treatment programs. Drug resistant strains may be spread to the general population.

A high rate of attrition from treatment programs thus poses a challenge to program implementers and constitutes an inefficient use of valuable and often scarce resources. The cost of running ART programs may increase due to the need for second-line and salvage regimens, which are more expensive. Second line regimens also pose adherence challenges due to pill burden and frequency and severity of side effects. The issue of retention of patients in ART programs therefore is of public health importance.

Aim and Objectives of the Study

The aim of the study is to analyze the reported cases of HIV/AIDS patients undergoing Antiretroviral Therapy (ART) programme at Sir Yahaya Memorial Hospital (SYM), Birnin Kebbi, Kebbi State, Nigeria. To achieve this aim, the following objectives are formulated:

- i. To fit least squares trend models to the data of patients undergoing ART programme at Sir Yahaya Memorial Hospital, Birnin Kebbi.
- ii. To use the models developed to forecast future occurrences of the status under study
- iii. To determine whether the current status of patients is dependent on sex and age group.

Research Hypotheses

1. H_0 : The current status of patients under study is independent of sex
2. H_0 : The current status of patients under study is independent of age group

Literature

The advent of antiretroviral therapy (ART) has changed the course of the epidemic and made HIV a chronic illness rather than a death sentence. However, with Antiretroviral therapy comes a lot of responsibilities for the patient, care provider and the community as a whole: particularly, long-term adherence to treatment if the therapy is to work well and minimize the possibilities of drug resistance developing Hassman, (2007); Kapiriri, L., Robbestad, B. & Norheim, O. F. (2001). This demands that when patients join antiretroviral therapy programs, long-term retention is sustained.

For ART to work, HIV infected individuals whose immune systems have been damaged need to take the medications regularly as life-long treatment. If people taking Antiretroviral Drugs (ARVs) stop taking their medications, they may get sicker or die, or the virus that they carry may become resistant to the antiretroviral drugs. Yet the second- line regimens are expensive and carry potential for more adverse drug reactions.

The advent of antiretroviral therapy (ART) has transformed HIV/AIDS into a chronic disease characterized by enhanced quality of life and increased life expectancy. In countries with limited resources, expanded availability of ART through funding from the President's Emergency Plan for AIDS Relief (PEPFAR), the Global Fund and other initiatives is extending treatment benefits to citizens living with HIV in these settings. While access to treatment must be increased to achieve the Emergency Plan goal of providing ART to two million individuals in 15 focus countries by 2008, maintenance on prescribed therapy with an unprecedented high level of adherence for the lifespan of the individual is critical for optimal viral suppression and clinical outcomes. These outcomes are required to safeguard the treatment gains made possible by the Emergency Plan and other funding opportunities (Kapiriri *et al*, 2001).

Research from developed countries reveals that incomplete adherence and early treatment discontinuations are among the strongest predictors of virological failure, drug resistance and mortality among HIV positive individuals (Paterson, DL, Swindells S, Mohr J and Brester M, 2000; Bangsberg, D.R, Hech, t F.M and Charlebois, E.D.2016;). Medication adherence focuses upon maintaining the therapeutic medication regimen and is described as taking the correct drug in the correct dose with the correct frequency at the correct time. To achieve undetectable levels of the virus in the blood and prevent the development of drug-resistant virus, patients are required to maintain consistently high levels of adherence (British HIV Association, 2005).

Achieving these levels of adherence presents significant challenges for both patients and health care providers. Once initiated, ART is a life-long treatment, consisting of multiple medications to be taken with varying dietary instructions. These medications have side effects, some of which may be temporary while others may be permanent or may require a change of medications (Caplan, R.A., Posner, K. L. & Cheney, F. W, 2013).

In addition to therapy-related factors, other variables can contribute to adherence (or non-adherence), including socio-demographic factors (e.g. gender-related roles and family and social support), psychological factors (e.g. depression), disease characteristics (e.g. duration of HIV infection and opportunistic infections), and patient/provider and health system-related elements (Nieuwkerk, P T, Sprangers, M.A.G and Burger, D.M., 2001)

While the predictors and biologic consequences of adherence to ART are well documented in developed countries, information from resource-poor settings is limited. Retention is a critical determinant of adherence as patients must be actively attending and participating in an ART program in order to receive their medication and to have their HIV clinical indicators monitored (Paterson, *et al*., 2000)

A prospective study conducted in South Africa provided some important findings regarding death and non-death losses among 927 patients attending an ART program. Overall, this study found that loss to follow-up and late mortality rates among ART patients (death after 4 months of ART treatment) were low, reflecting good retention in the program and good treatment

response. This study, however, followed a cohort of patients in an ART program with community-based counselors who traced patients if they missed an appointment (DeOlalla P, Knobel, H, Carmona A, Guelar A, and Lopez-Colomes J, (2007).

ART-scale up must be accompanied by decentralization of treatment to the most peripheral level. Appropriate systems need to be created to accommodate the ever-increasing patient load. This includes capacitating all levels of healthcare workers to deliver and monitor ART and ensuring additional adherence support by non-medical staff (Sydney R., Matthew F.P., and Christopher J.G., (2007).

Since early 2007, there have been growing concerns that although most people initiating antiretroviral therapy in resource limited settings are doing well on their first-line regimen, an unacceptably large and increasing proportion of patients are being lost to follow-up and care, even at model sites, as facilities reach the limits of the number of subjects they can easily manage (Sydney, et al., 2007).

According to AIDS Research report of November, 2009, there are inadequate retention rates in Sub-Saharan Africa ART Programs. They found that only slightly more than 60 percent of patients enrolled in antiretroviral treatment (ART) programs in sub-Saharan Africa continued treatment two years after treatment initiation. In addition, findings indicated that 40 percent of patients who stopped ART died within two years. The study, which collected data on 13 sub-Saharan African countries, provides insights into program initiation and retention rates. It also raises concerns regarding future policies, program implementation, and resource allocation for ART protocols in resource-poor settings.

According to this study, the development of an effective tracking system to reduce the proportion of patients lost to a lack of follow-up is a critical requirement for ART programs. Furthermore, improvements in the development and integration of community-based approaches and national strategies for testing, treatment, and care need to be made to ensure increased patient retention rates and continued funding—of ART programs in sub-Saharan Africa. (Richardson, 2009).

Materials and Methods

The Study Area

This study was conducted in Sir Yahaya Memorial Hospital (SYMH), Birnin Kebbi. Sir Yahaya Memorial Hospital (SYMH), Birnin Kebbi, Kebbi State, Nigeria, is the premier hospital in the State. It was established in 1952 by the native authority (NA) with native authority funds on the initiative of the then 17th Emir of Gwandu, Sir Yahaya Haliru Abdu. It was commissioned in December 1952 as a general hospital. When Kebbi state was created in 1991, the hospital was made the state specialist hospital.

Data Collection

The secondary data used for this study was obtained for a period of 58 weeks from 5/12/2017-8/01/2019 from the HIV/AIDS patients undergoing antiretroviral therapy (ART) programme

in the study area. The data was collected from registers, patient's case folder and patient's management and monitoring forms (PMM forms) which are produced and supplied by global HIV/AIDS initiative Nigeria (GHAIN)/ USAID providing us with detailed information about the patients on ART programme, date of enrollment, sex, age and current status in Sir Yahaya Memorial Hospital, Birnin Kebbi.

Participants

The population of 390 patients comprising all categories of patients in antiretroviral therapy clinic in Sir Yahaya Memorial Hospital, Birnin Kebbi. Which includes patients who have defaulted from ART programme, both males and females and of different age groups; patients who are dead while receiving ART services, both males and females and of different age groups and patients (in-care) undergoing ART programme, both males and females and of different age groups.

Data Analysis and Results

To analyze the collected data, trend analysis of time series data using the method of least squares and chi-square test of independence were used. The analyses were performed using statistical software package Minitab for windows.

The method of least squares is a mathematical method and with its help, a trend line is fitted to the data in such a manner that the following two conditions are satisfied by the trend line given by $Y_t = b_0 + b_1 t + e_t$

1. $\sum(Y - Y_c) = 0$ i.e. the sum of the deviations of the actual values of Y and the computed values of Y is zero.
2. $\sum(Y - Y_c)^2$ is least, i.e. the sum of the squares of the deviations of the actual values and the computed values is least.

The line obtained by this method is called as the "line of best fit"

The two normal equations used are:

$$\begin{aligned} \sum Y &= na + b \sum Y \\ \sum tY &= a \sum t + b \sum t^2 \end{aligned}$$

Where t is the time period and Y is the value of the item measured against time, β_0 is the Y-intercept and β_1 is the coefficient of t indicating slope of the trend line i.e. represents the average change from one period to the next and e_t the error term.

Suppose that in a particular sample a set of possible events $E_1, E_2, E_3, \dots, E_k$ are observed to occur with frequencies $o_1, o_2, o_3, \dots, o_k$ called observed frequencies and that according to probability rules they are expected to occur with frequencies $e_1, e_2, e_3, \dots, e_k$ called expected or theoretical frequencies. Often we wish to know whether the observed frequencies differ significantly from the expected frequencies

A measure of the discrepancy existing between the observed and expected frequencies is supplied by the statistic χ^2 (read chi-square) given by

$$\chi^2 = \frac{(o_1 - e_1)^2}{e_1} + \frac{(o_2 - e_2)^2}{e_2} + \dots + \frac{(o_k - e_k)^2}{e_k} = \sum_{j=1}^k \frac{(o_j - e_j)^2}{e_j} \quad (1)$$

Where if the total frequency is N,

$$\sum o_j = \sum e_j = N \quad (2)$$

An expression equivalent to formula (1) is

$$\chi^2 = \sum \frac{o_j^2}{e_j} - N \quad (3)$$

If $\chi^2 = 0$, the observed and theoretical frequencies agree exactly; while if $\chi^2 > 0$, they do not agree exactly. The larger the value of χ^2 , the greater is the discrepancy between the observed and expected frequencies.

The collected data for 54 weeks was analyzed and the following results are obtained:

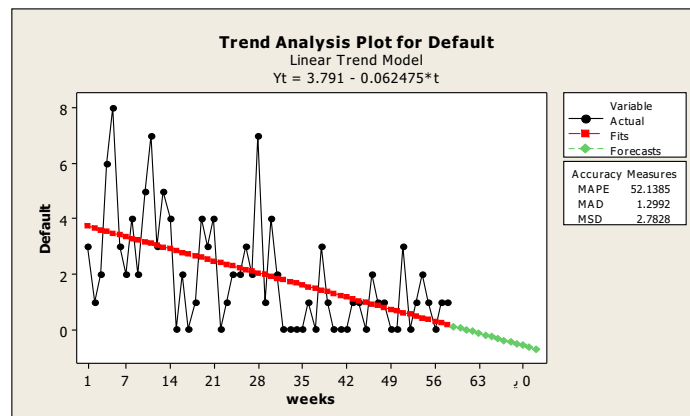


Figure 1: Trend Analysis Plot for Defaulted Patients.

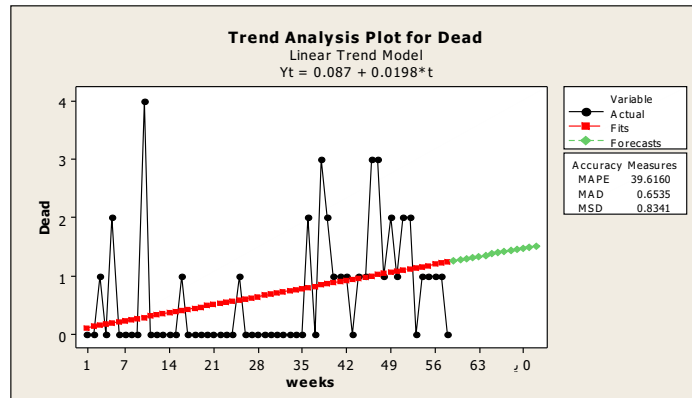


Figure 2: Trend Analysis Plot for Dead Patients.

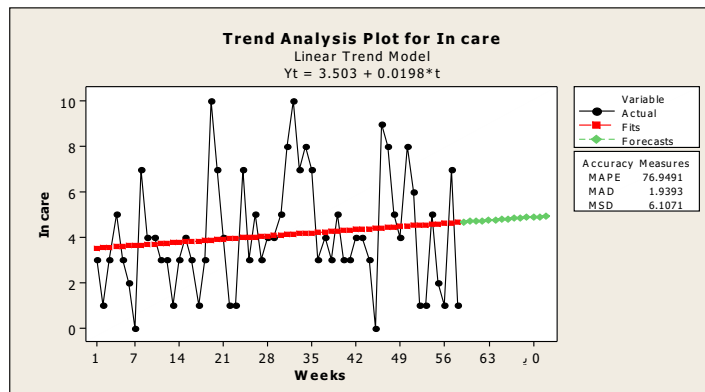


Figure 3: Trend Analysis Plot for in care Patients.

For the chi square test for independence testing whether the current status of patients is independent, the results yielded ($\chi^2 = 1.909$, $DF = 2$ and $P = 0.385$). The corresponding test to determine whether current status of patients is independent of age group however the chi square results were ($\chi^2 = 0.491$, $DF = 4$ and $P = 0.974$).

Discussion of Results

The graph of the original data indicated an irregular trend pattern for all the three categories of the cases of HIV/AIDS at the hospital with upward and downward movement of the series in the period under study as shown in Figures 1, 2 and 3. The fifth week has the highest number of defaulted patients when 8 cases were recorded while the 10th week has the highest number of death with 4 people and the 19th and 32nd weeks had the highest number of in care patients with up to 10 cases recorded during the period.

Three functional linear models one each for defaulted patients, dead patients and patients in care were fitted to the collected data and forecast were made on the basis of these models. Results obtained revealed a weekly decrease in the number of default patients which will likely be 0 by the 3rd week of January, 2019. However, an increase was observed in the number of

dead and in care patients for the next 14 weeks which implies that the two are likely going to be on the increase though more pronounced in case of in care patients if mitigating measures are not put in place with 2 and 4 cases to be recorded for dead and in care patients by the third week of January 2019.

The Chi-square test for independence results showed that the current status of patients under study is independent of the sex of patients since the p-value obtained (0.385) is greater than the level of significance which is 0.05. Also the test revealed that current status of patients under study is independent of age group since the p-value obtained (0.974) is greater than the level of significance which is 0.05.

Conclusion

On the basis of the results obtained, it can be concluded that if the current trend of antiretroviral therapy is maintained, the recorded number of default patients will be on the decrease while the number of dead and in care patients will be on the decrease. Also, it can be concluded that the current status of patients undergoing antiretroviral therapy (ART) programme at the hospital is independent of their sex and age group.

Recommendations

By considering the importance of HIV/AIDS patients' retention to ART programme and various short comings that can hinder the effectiveness of the programme, the following recommendations are made:

1. Electronic data base and system networking should be installed to enable those involved in the patients care to record information electronically and link all the systems. This will enhance easy retrieval of patient's information by both clinician and other health workers for present and future references.
2. There should be more training and workshop/Seminar to educate health care providers, so that relevant documents can be properly filled in obtaining information for sound decision making in the treatment of HIV/AIDS patients.
3. Good contact tracking methods be employed by increasing the financial resources to serve as incentive for contact tracking team. This will enable the members of the team to identify those who lost follow-up in order to counsel them on drugs adherence, as failure to adhere on treatment will affect the efficiency of the treatment, more over information about some patients that died can be traced through contact tracking services.

Reference

- Bangsberg, D. R, Hech, T. F. M & Charlebois, E. D (2016). Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. *J Infect Dis. 1210 Suppl 1* S111–S117.
- British HIV Association (2005). *HIV treatment guidelines*, British HIV Association 2005.
- Caplan, R.A., Posner, K. L. & Cheney, F. W. (2013). Effect of outcome of physician judgments of appropriateness of care. *Journal of the American Medical Association*, 167, 567-572.
- DeOlalla P, Knobel H, Carmona A, Guelar A, Lopez-Colomes J, & Cayla J., (2007). Impact of adherence on highly active antiretroviral therapy on survival in HIV-infected patients. *Health Policy*, 96, 262-264.
- Federal Ministry of Health (2011). *Federal ministry of health, Nigeria. Comprehensive EPI Multi-Year Plan, 2011–2015*. Abuja, Nigeria (2011). Available at: http://www.nationalplanningcycles.org/sites/default/files/planning_cycle_repository/nigeria/cmyp2011-2015_country_final.pdf.
- Hasman, A. (2007). Accountability for reasonableness: Opening the black box of process. *Health Care Analysis*, 13, 261-273.
- Kapiriri, L., Robbestad, B. & Norheim, O. F. (2003). The relationship between prevention of mother to child transmission of HIV and stakeholder decision making in Uganda: Implications for health policy. *Health Policy*, 66, 199-211.
- Nieuwkerk P.T, Sprangers M.A.G & Burger D.M., (2001). Limited Patient adherence to Highly Active Antiretroviral Therapy for HIV-1 infection in an observational Cohort Study, The burden and costs of chronic diseases in low-income and middle-income countries. *Lancet*, 370, 1929-38.
- Paterson, D. L, Swindells, S, Mohr, J, Brester, M, Vergi,s E. N, Squier, C., (2000). *Adherence to protease inhibitor therapy and outcomes in patients with HIV infection*. 6th Conference on Retroviruses and Opportunistic Infections; 1998.
- Richardson, E. K. (2009). The antiretroviral rollout and drug-resistant HIV in Africa: Insights from empirical data and theoretical models. *Journal of Health Services Research & Policy*, 14, 234-242.
- Sydney R., Matthew F. P., & Christopher J. G., (2007). Patient retention in antiretroviral therapy programs in Sub-Saharan Africa. A Report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. *Value in Health* 14(4) 403-413.
- USAID (2016). The Lives Saved Tool (List) Manual. *Health Policy Initiative*,
- WHO/UNAIDS (2017). *Health workforce innovative approaches and promising practices: Study Providing Doorstep Services to Underserved Rural Populations: Community Health Officers in Ghana*. Capacity Project USAID.