ORIGINAL ARTICLE

Time Trend of the People lost follow up on Antiretroviral Therapy (ART) Services in Nepal: A Epidemiological Modelling

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Citation

Article Cycle

Abstract

Background: The real state about the spread of the HIV epidemic in Nepal is not clear since the details available are on the basis of repeated integrated biological and behavioral surveillance. **Objective** To study the trends of People lost follow up on ART in future. **Material and methods**: A retrospective study was carried out on the data collected from the Health ministry records of Nepal, between 2006 and 2012. Descriptive statistics and statistical modelling were used for the analysis and forecasting of data. **Results:** Including the constant term from the equation, the quadratic model was the best fit, for the forecasting of People lost follow up on ART. Using quadratic equation, it is estimated that 4331 reported number of People lost follow up on ART will be there in Nepal by the year 2020. **Conclusion:** The People lost follow up on ART in Nepal are having an increasing trend. Estimates of the total number of People lost follow up on ART attributable to the major routes of infection make an important contribution to public health policy. They can be used for the planning of healthcare services and for contributing to estimates of the future numbers with People lost follow up on ART used for planning health promotion programmes.

Key Words

Introduction

The current situation of HIV in Nepal is different from when the first case was diagnosed in 1988. Up until recently, (2013) the total number of positive cases reported are 22, 994 out of which 1055 people lost follow up on Antiretroviral Therapy (ART). Nepal is low prevalence country for HIV and AIDS (<1 percent). The real state about the spread of the HIV epidemic in Nepal is not clear since the details available are on the basis of repeated integrated biological and behavioural surveillance and it may not represent the prevalence rate of the general population. [1,2] ART started in Nepal in February 2004 from Teku Hospital. Government is providing free of cost ART service to all those in need. There are forty four ART centers in Nepal. CD4 count service is available in 17 sites. National ART guidelines were revised in 2012. [1] The capability of mathematical and statistical models in understanding and predicting epidemics had been

proved by the study conducted by Kermack and McKendrick (1927) for treatment of the Bombay plague of 1905–06. Anderson and May (1991) came up with more models of infections including HIV with illustrations. One of the earliest Indian attempts at modeling data on AIDS had been done by Mukerji (1989). [3-5] This model used annualized south Asian regional data and extrapolated to AIDS in future. Basu et al (1998) attempted to model the spread of AIDS in a comprehensive manner with limited data. [6] The applicability of various models to predict AIDS in India, beginning from classic simple epidemic models to more complex heterosexual transmission models proposed and back calculation method were done by Rao S (2003). [7] Williams (2005), et al studied about HIV prevalence in India. Joshua (1999), et al studied methods for modeling the HIV/AIDS epidemic in Sub Saharan Africa. [8,9] Sathian B et al (2011) used curve fitting method as a powerful tool to forecast the reported number of HIV cases in Nepal. [10] Until the

last decade conventional study through statistical methods were adopted to understand the trend and prevalence of HIV/AIDS in almost all countries.

Aims & Objectives

The objective of the study is to find out the trends of people lost follow up on ART in future.

Material and Methods

We conducted a secondary data analysis of the People lost follow up on ART (cumulative) data between 2006 and 2012, Nepal. The survey was conducted under the administrative supervision of the population division of the Ministry of Health and Population (MOHP) and it is available in the National Centre for AIDS and STD Control (NCASC) website (http://www.ncasc.gov.np/index.php) [1, 2].

The data was analysed using Excel 2003, R 2.8.0, Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA) and EPI Info 3.5.1 windows version. A p-value of < 0.05 (two-tailed) was used to establish statistical significance. The annual reported numbers of People lost follow up on ART (cumulative) plotted in y-axis against the corresponding year in the x-axis. Curve fitting, also known as regression analysis, was used to find the "best fit" line or curve for a series of data points. Linear, Logarithmic, Inverse, Quadratic, and Cubic were chosen to fit to the obtained curve. F-test was used for selecting the best fitting curve for the testing of hypothesis. P-value was taken as significant when < 0.05 (two-tailed). R^2 value > 0.80 was taken as significantly better for prediction [10]. The decision regarding the selection of a suitable prediction approach is governed by the relative performance of the models for monitoring and prediction. It should also adequately interpret the phenomenon under study. Quadratic model selected here could closely fit curves for estimated and reported people lost follow up on ART cases (Figure 1). While building model, the extremities (maximums and minimums) play a great role. If the points are scattered more, the curve tries to adjust with maximum number of observed points. The quadratic model is a second degree polynomial, represented by the equation $y = m_0 + m_1 * x + m_2 * x^2$, where m0 is the constant term and m1 and m2 are coefficient terms. [11,12] Where Y is the number of number of reported People lost follow up on ART (cumulative) annually and X is the corresponding year; 1=2006, 2=2007, 3=2008, 4=2009 and so on.

Results

The data was modelled using the curve fitting method. [Tables 1 and Graph 1] depicts the model summary and the parameter estimates including the constant term for different models. Including the constant term in the equation, the quadratic model

was the best fit, for the forecasting of People lost follow up on ART. The quadratic model equation below (1) contain X and Y, which are the corresponding year and frequency of reported People lost follow up on ART respectively. m_1 and m_2 calculated from the observed data.

Discussion

Modelling and Extrapolation: A plot is a graphical representation of the collected data (independent and dependent variables) involved in a study. The association between these variables are then assessed by connecting the `points' with a line. Though very true, this association cannot be relied upon to predict the future trend of this data. Now a `model', which `fits best' to the observed data has to be worked out. This is then `fitted' and used to replace the existing set of data points as `the appropriate model'. After `modelling' the observed data, this model can be used to predict future trend of the dependent variable for a given change in the other. The foregoing statement covertly mentions several requirements which often ensure confident achievement in any subsequent extrapolation from the model. The model selected must be the most appropriate for the collected data. A usable and understandable curve-fitting method is to be available from which the model facts those are reflective of future behaviour can be obtained. [13,14] Timely and accurate monitoring of the HIV epidemic requires measures of incidence, that is, the number of new infections in a defined population that occur during a defined time period. Unfortunately, longitudinal studies that have traditionally provided incidence measures are costly, time consuming, logistically complex, and may be subjectively biased, differential loss to follow-up, or an intervention effect. [15] As a result, public health agencies have generally relied on surveys that measure HIV prevalence, the proportion of persons at a specified point in time that are infected, to track the epidemic [16].

Using the curve fitting method, we estimated the number and trend of reported People lost follow up on ART at Nepal from the year 2006 to 2020. Quadratic model provided closely fitted curves for estimated and reported People lost follow up on ART (Graph 1). While building model, the extremities (maximums and minimums) play a great role. If the points are scattered more, the curve tries to adjust with maximum number of observed points. Therefore, it might give over- and under-estimation inevitably, but that is not the case in all the situations. In our study cubic model was having more R^2 value compared to quadratic model. But while forecasting the annual reported People lost follow up on ART, cubic model gave over estimated values in comparison with quadratic model. A sudden annual

decrease and increase in the trend is possible, as the curve cannot exactly connect these data points because of its shape. For adjusting the over-and under-estimation, the model gave wide confidence intervals in case of some years (Table 2). In our study, the future annual reported People lost follow up on ART (Table 2) shows an increasing trend. As of 2013, national estimates indicate that there are 22, 994 reported number of HIV cases and 1055 people lost follow up on ART in Nepal, which is close to the prediction done by our study. [1,2] Mathematical models are useful in a number of ways. Because of the complexity and the seriousness of the disease, mathematical models of the HIV epidemic and HIV pathogenesis are especially important for a number of reasons. Mathematical models of the HIV epidemic and HIV pathogenesis can be used to provide in depth understanding of some basic features and principles of the HIV epidemic and HIV pathogenesis; it will help reveal consequences of important parameters of the HIV epidemic and HIV pathogenesis. One may use mathematical models of the HIV epidemic to assess impacts of many risk factors and to screen for important risk variables for purposes of prevention and control of AIDS. [17] Mathematical models of the HIV epidemic can also be used to evaluate and compare different strategies of prevention and control of AIDS. [18] One may use mathematical models of the HIV epidemic to project future People lost follow up on ART. [19] Sathian B et al. used curve fitting method as a powerful tool to forecasts communicable and non-communicable disease trends in Nepal. [10-14, 20] Our study hereby establishes the applicability of statistical modelling in predicting the reported number of People lost follow up on ART in the Nepalese context.

Adherence to ART regimen is crucial for the management of HIV infection and studies have shown that cumulative adherence of <90% can results in less successful suppression of the viral load. Poor compliance and lost to follow up leads to sub therapeutic drug concentrations of prescribed medications enhancing development of resistance. [21] Lost to follow up has become one of the barriers in the management of infants and children for various reasons. Combination antiretroviral regimens require multiple daily doses and are often unpalatable, requiring extreme dedication on the part of the care provider and child. Active Participation of the guardians for the decision to initiate and continue ART is essential for adherence of infants and children. [22] Although prevention of mother-to-child HIV transmission (PMTCT) programs are widely implemented, many children do not benefit from them because of loss to follow-up (LTFU) leading to increased risk of vertical transmission to new-borns. Measures directed to mothers to prevent LTFU also improve the follow up care of infants and childhood.

ART in relation with mortality and follow up was studied in large clinic of Uganda using a sampling-based approach. Lost to follow-up revealed accounted for the suboptimal speed and the completeness of ART initiation. Improving the kinetics of ART initiation was suggested to make ART more in real-world populations of Africa. [23] Improving adherence requires a supportive environment; accessible treatment; clear instructions about regimens; and regimens tailored to individual patients' lifestyles. Healthcare workers should address some of the practical and cultural issues around ART medicine whilst policy-makers should develop appropriate social policy to promote adherence among ART-prescribed patients. [24] Intensive education on the relationship of drug adherence to viral suppression, training on drug administration, frequent follow-up visits, and commitment of the caregiver and the patient (despite the inconvenience of side effects, dosing schedule, and so on) are critical for successful antiviral treatment.

Conclusion

The People lost follow up on ART in Nepal are having an increasing trend. Estimates of the total number of People lost follow up on ART attributable to the major routes of infection make an important contribution to public health policy. They can be used for the planning of healthcare services and for contributing to estimates of the future numbers with People lost follow up on ART used for planning health promotion programmes.

Recommendation

NCASC should introduce refresher [training] courses on data recording, reporting and monitoring of People lost follow up on ART with the help of International expert's team which include clinicians, public health professional and biostatistician. NCASC can also plan for the electronic reporting system like other developed counties are following. Introduce extra incentives to efficient and hard- working staff members. Encourage all service providers on the timely reporting of accurate data. NCASC should consider revising the allocation of budget under different headings so that it can be used more appropriately.

Authors Contribution

BS: Conceptualized the research, planned and conducted the data analysis, interpreted the results, wrote the first draft of the manuscript for publication and is the guarantor; SA and JS: Conceptualized the research, co-drafted the first draft of the manuscript

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Tables

TABLE 1 MODEL SUMMARY AND PARAMETER ESTIMATES INCLUDING THE CONSTANT TERM FOR DIFFERENT MODELS FOR THE REPORTED NUMBER OF PEOPLE LOST FOLLOW UP ON ART

| Equation	Model Summary		
	R Square	F value	p-value
Linear	0.942	81.1587	0.0001
Logarithmic	0.765	16.2987	0.010
Inverse	0.527	5.56945	0.065
Quadratic	0.997	747.5875	0.0001
Cubic	0.998	441.0644	0.0001
Compound	0.953	101.885	0.0001
Power	0.968	153.4808	0.0001
S	0.832	24.7325	0.004
Growth	0.953	101.885	0.0001

Exponential	0.953	101.885	0.0001

The equation for the quadratic model for the reported number of People lost follow up on ART is Y= 26.857-17.357 X +20.286X² --------- (1)
(Where Y is the number of number of reported People lost follow up on ART annually and X is the corresponding year; 1=2006, 2=2007, 3=2008, 4=2009 and so on)
Using the equation (1), reported numbers of People lost follow up on ART were estimated.

TABLE 2: REPORTED NUMBER OF PEOPLE LOST FOLLOW UP ON ART UP TO THE YEAR 2012, AND ESTIMATED NUMBER OF PEOPLE LOST FOLLOW UP ON ART CASES UP TO THE YEAR 2020.

Year	Estimated cases	Predicted cases	Lower Limit	Upper Limit
2006	32	30	0	105
2007	54	73	9	138
2008	182	157	93	222
2009	293	282	217	347
2010	426	447	383	511
2011	647	653	589	717
2012	908	899	824	975
2013		1186	1081	1291
2014		1514	1361	1667
2015		1882	1665	2098
2016		2291	1996	2585
2017		2740	2354	3125
2018		3230	2740	3719
2019		3760	3154	4366
2020		4331	3595	5066

Figures

GRAPH 1: FITTED CURVES FOR REPORTED PEOPLE LOST FOLLOW UP ON ART
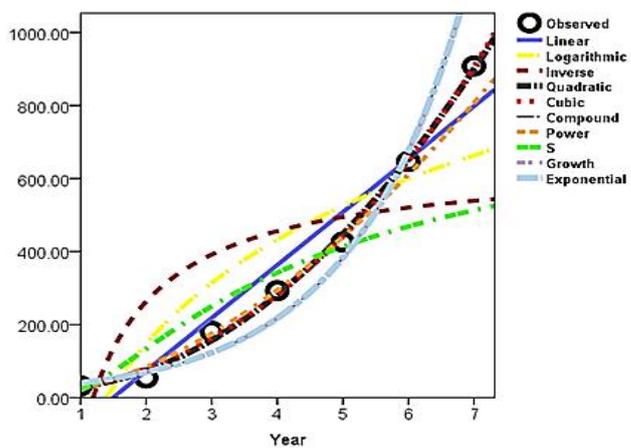
(X-axis shows years; 1=2006, 2=2007, 3=2008, 4=2009 and so on, Y-axis shows number of people lost follow up on ART)