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Original Article

Predictors of first line antiretroviral therapy failure and burden of second line antiretroviral therapy

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ABSTRACT

Background: As HIV steps into the third decade, there are more number of patients living on lifelong (antiretroviral therapy) ART and facing the threat of drug resistance with subsequent treatment failure. The aim of this study was to determine predictors of first-line ART failure with the objectives to estimate the burden of 2nd line ART.

Methods: A retrospective 5-year cohort of HIV patients who were initiated on first line ART in 2008–09 was studied. Patients were followed from the time of ART initiation. Kaplan–Meier methods and Cox proportional hazards regression models were used to estimate probabilities and predictors of first line ART failure.

Results: Of the total of 195 patients initiated on first line ART, 15 patients were switched to second line ART yielding 7.69% failure rate. During the 7178 person-years of follow-up, the incidence of first line ART failure was 2.09 per 1000 person-years. The Kaplan–Meier survival analysis gave a mean survival time of 55.6 months. BMI, CD4 count at ART initiation and presence of opportunistic infections were significant predictors of first line ART failure. The burden of second line ART patients by the end of 5 years of first line ART is expected to be 151 patients.

Conclusion: Though the first line ART failure is quite low in this study, we still need to be vigilant for lower BMI, low baseline CD4 count and occurrence of opportunistic infections to efficiently manage failures on first line ART.

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Introduction

The HIV epidemic is widely acknowledged to be a most severe health crisis of modern times. There is no cure and no vaccine. In absence of any cure, antiretroviral therapy (ART) is the only treatment that inhibits HIV. ART has changed the HIV disease to a manageable chronic condition by suppressing the viral load, increase in CD4 count and partial restoration of the immune function.[1] Though the introduction of HAART has led to an increase in survival among HIV-infected patients, decreased HIV-associated morbidity and mortality, and improved quality of life among HIV patients, it is seen that a considerable proportion of patients fail to achieve a sustained virological response to therapy.[2] As ART uptake increases resistant viruses develop leading to treatment failure. As a result of failure patients need to be shifted to second-line regimen to suppress viral load.[3,4] Of the total HIV patients on ART, around 2% are on a second-line regimen.[5] Literature from South Africa estimated a high failure rate of 14% by 5 years on ART.[6] Experience from the TREAT Asia HIV Observational database (TAHOD) showed that the rate of clinical failure on this regimen was 7.3 per 100 people – years.[7] HIV surveillance in the armed forces promulgated by the HIV/AIDS policy of O/o DGAFMS and which is in consonance with the national policy promulgated by National AIDS Control Organisation, MoHFW is more systematic and efficient because of Advanced Immunodeficiency centres (AIDC), Immunodeficiency centres (IDC) and First Line Immunodeficiency centres (FIDC). However we still do not have the estimates of the patients requiring second line drugs.

In light of the above facts the primary objective of the paper was to estimate the incidence of first line ART failure and study its associated predictors. The secondary objective was to estimate the burden of second line ART.

Materials and methods

A cohort study of HIV-infected persons more than 18 years of age who were initiated standard first line ART in ART Centre of Pune in 2008–09 was undertaken. The study flow chart is given in Fig. 1. Administered ART drug regimen was as per government guidelines. The patients eligible were those with minimum of 6 months of follow-up and the study follow-up time was maximum of 5 years. Data on patients demographic variables and treatment information were gathered from individual case sheets and ART registers. Patient follow-up began on the date of ART initiation. Dependent variables considered were antiretroviral treatment failure and time to the occurrence of treatment failure. Predictors considered as independent variables included age, years since HIV diagnosis, weight at baseline, hemoglobin, CD4 at baseline, TB treatment and adherence of the patients. Ethical clearance was obtained from the institutional ethics committee. All the information obtained was kept in a confidential manner. Patient names were delinked to the results of the study.

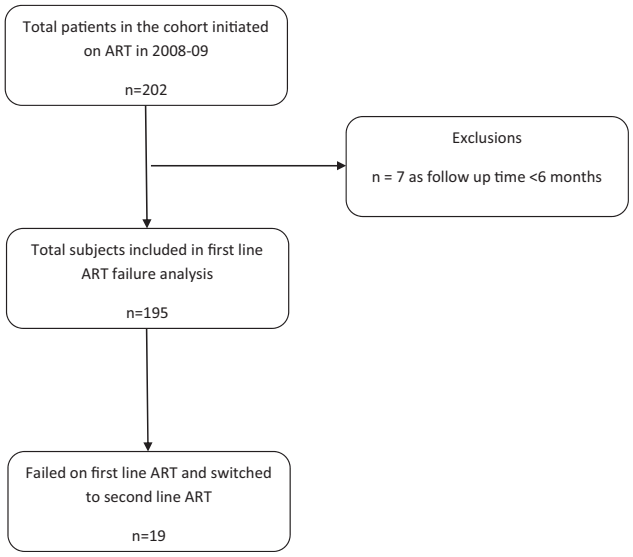

Fig. 1 – Study flow chart of first line ART failure and switch to second line ART.

Statistical analysis

Failure analysis with failure rate and incidence per 100 person-years of follow-up were calculated. Incidence (hazard) rate was defined as number of new cases of disease per population at-risk per unit time (or mortality rate, if outcome is death). Time-to-event analysis was performed using the outcome of switch to second-line ART. Censoring is done if patient died, got posted out from the unit or after 60 months from ART initiation. The significance of the quantitative variables in the two groups namely first line ART failure and no failure was tested using unpaired t test and qualitative variables using chi square test. All variables, which were attested significant by t test or chi square, were only further subjected to the multivariate analysis using Cox proportional hazard model. The survival rates and year-wise survival probabilities were determined. Kaplan–Meier survival estimates and hazard ratios (HR) defined as ratio of incidence rates, using Cox proportional hazards regression model were used to analyze predictors of the first line ART failure and second line ART switch. All analyses were done using SPSS software, version 22.0 (SPSS) (Fig. 2).

Results

Baseline patient characteristics for complete cohort

A total of 202 patients, of whom 195 HIV patients >18 years of age and all male patients who were initiated on first line ART in 2008, were eligible in the study with more than 6 months of follow-up. These 195 patients contributed 7178 person-years follow-up. The mean age of the patients was 36.54(SD = 7.69). Majority of the patients (65%) were from the age group of 25–45 years of age. Most of the subjects were secondary educated (76.3%) and 93.16% were married. Probable mode of transmission was heterosexual mode for 57% and for remaining 43%