International Journal of Advances in Medicine
Shidhaye P et al. Int J Adv Med. 2021 Aug;8(8):1193-1200
http://www.ijmedicine.com
pISSN2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20212866

Original Research Article

Virological failure among HIV infected individuals on antiretroviral therapy in Pune, India: a cross-sectional study

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Received: 23 March 2021
Accepted: 29 April 2021

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ABSTRACT

Background: It is important to identify and manage determinants of virological failure among HIV infected individuals on treatment for achieving viral suppression. This study aimed to identify proportion and factors associated with virological failure among HIV infected individuals receiving first line antiretroviral therapy (ART).
Methods: A total of 2670 adult HIV infected individuals attending ART centre at ICMR-National AIDS Research Institute, between January 2005 and June 2019 and having their recent viral load done after implementation of guidelines on routine viral load testing were included. Data were reviewed and analysed.
Results: Of the 2670 people living with HIV (PLHIV) on first line antiretroviral therapy, 48% were male and 69% were more than 40 years of age. Mean baseline CD4 count at ART initiation was 252 cells/mm^3 (SD:210, IQR 116-313) Overall, 13% (340/2670) of the participants showed virological failure. In multivariate analyses, participants with younger age and males retained significant association. Those with baseline CD4 counts of less than or equal to 500 cells/mm^3 at treatment initiation (adjusted OR 1.71; 95% CI 1.08-2.70; p=0.022) and ART adherence ≤95% within last three months of recent viral load determination (adjusted OR 1.55, 95% CI of AOR 1.04-2.32; p=0.031) had higher risk for virological failure as compared to others. PLHIV with ART substitution due to various reasons were almost twice as likely to have virological failure (adjusted OR 1.83, 95% CI 1.44-2.33; p<0.001).
Conclusions: It is crucial to focus on factors leading to virological failure among HIV infected individuals attending ART centre. Early linkage to treatment and ART initiation along with adherence counselling at every follow up visit play an important role in mitigating virological failure.

Keywords: Virological failure, people living with HIV, ART, India

INTRODUCTION

HIV is a major public health problem with 2.14 million estimated people living with HIV (PLHIV) in India and around 1,133,950 are on treatment under national program in 532 antiretroviral therapy (ART) centres by August 2017.[1] The Indian National AIDS Control Programme (NACP) is committed to an ambitious treatment target of UNAIDS 90-90-90, which aims at 90% of all people living with HIV know their PLHIV status, 90% of all PLHIV with diagnosed HIV infection to receive sustained ART and 90% of all those receiving ART to achieve viral suppression.[2] Treat all strategy was adopted to provide ART to all PLHIV irrespective of their CD4 counts and routine viral load (VL) monitoring was introduced by the NACP.[3] The objective of introducing routine viral load monitoring in the national programme was to provide early and accurate indication of treatment failure, assess need to switch the treatment regimen, thus thereby reducing the accumulation of drug resistance mutations and improving treatment outcomes.[3]

High viral load findings indicate non-adherence and help identifying PLHIV who need ART adherence support.[4] Implementation of enhanced adherence strategies for PLHIV with detectable viral load are important for further virological suppression.[5]

Current test and treat approach under NACP and routine viral load monitoring guidelines have increased the viral load testing. It is anticipated that demand for viral load tests will increase to 28.5 million by 2021, reflecting on the increase in the number of individuals who will receive antiretroviral therapy.[2,3] Though there are many studies on treatment failure by using targeted viral load; there are few studies on virological failure from India after the introduction of routine viral load testing within programme.[5-9] With this background, the current cross-sectional study was conducted. The objective of this study was to determine the proportion and factors associated with virological failure among adult PLHIV on first line antiretroviral therapy attending ART centre located in Pune, India.

METHODS

Study design, setting and selection of participants

Current retrospective study was conducted by the Indian Council of Medical Research-National AIDS Research Institute (ICMR-NARI), located in the Pune district of the western state of Maharashtra, India. Records of PLHIV attending NARI ART centre, whose ART was initiated between January 2005 and June 2019 were considered in the study. The study was conducted after the implementation of National AIDS Control Organization (NACO) guidelines for routine viral load laboratory testing.[10] All those who had their recent HIV-1 viral load test done after the implementation of national guidelines were considered for study analyses.

Data collection

Records of all adult (≥18 year of age) PLHIV on first line ART regimen were reviewed and the recent HIV-1 viral load reports were considered. All PLHIV who had their HIV-1 viral load reports available after the implement-tation of national guidelines for VL were included in the study.[3] Data were extracted from the registers and files maintained at the ART centre. Those who were already diagnosed with failure, on the second line ART, those who were already diagnosed with failure, on the second line ART and transfer out were excluded from the study. and transfer out were excluded from the study. Sociodemographic and clinical profile of the participants were extracted from the national programme card. Information regarding age, employment, HIV confirmation test, past clinical history, CD4 count, ART regimen, ART regimen substitution, drug adherence, history of tuberculosis (TB) and other opportunistic infections were collected. The drug adherence was considered as above 95% if the average drug adherence of last three consecutive months before viral load testing was more than 95%. Blood samples were collected for viral load testing during their routine ART follow up visit and the HIV-1 viral load testing was carried out at the Metropolis laboratory and ICMR-NARI virology laboratory. This data were considered for analyses.

Viral load assay

HIV-1 plasma viral load was measured using quantitative real-time PCR HIV-1 viral load assay (Abbott molecular, Germany) at the Metropolis healthcare laboratory and the virology laboratory at ICMR-NARI within four hours of collection after processing.

Outcome variable

Virological failure, the outcome variable in the present study, was defined as plasma HIV-1 RNA more than or equal to 1000 copies/ml as per the national guidelines on viral load testing.[11]

Statistical analysis

The demographic and clinical characteristics of study participants were analysed by median and interquartile range (IQR) for continuous variables and by proportions for categorical variables. Univariate logistic regression analysis was performed to assess factors associated with virological failure. Variables with significant association ($p<0.05$) with outcome in univariate regression analysis were included in multivariate logistic regression model. Adjusted odds ratio (AOR) with 95% confidence intervals (95% CI) was calculated. Software package SPSS 20.0 (SPSS, Inc; Chicago, IL, USA) was used for data analysis.

RESULTS

Demographic and clinical profile

A total of 2670 HIV infected individuals were included in the study of whom almost half were males (48%, 1272/2670). The median age of the participants in our study at VL testing was 44 year (mean 44 year; SD:9.8; range 18-82 year, IQR 38.5-49.6) and two-third of the study participants, (69%, 1839/2670) were more than forty years age. Majority Of the total, 44% (1172/2670) study participants had completed secondary school and one-fifth never attended school or were illiterate (17%, 462/2670). One-tenth participants, 290 (11%) were unmarried, 59% (1581/2670) were living with their partners and one third PLHIV (30%; 808/2670) were unemployed. Heterosexual intercourse was the most common mode of HIV transmission (83%; 2225/2670). The mean baseline CD4 count at ART initiation among PLHIV was 252 cells/mm^3 (median 201 cells/mm^3, SD:210, range 1-1864, IQR 116-313).

Table 1: Virological failure and associated factors among PLHIV.

Variables	Total N=2670 frequency (%)	Virological failure N=340 (12.7%) frequency (%)	No Virological failure N=2330 (87.3%) frequency (%)	Crude Odds ratio (95%CI)	P value
Gender					
Male	1272 (47.6)	184 (14.5)	1088 (85.5)	1.35 (1.07-1.69)	0.011
Female	1398 (52.4)	156 (11.2)	1242 (88.8)	1	
Age (years)					
≤40	831 (31.1)	139 (16.7)	692 (83.3)	1.64 (1.30-2.07)	<0.001
>40	1839 (68.9)	201 (10.9)	1638 (89.1)	1	
Education					
Literate	2208 (82.7)	289 (13.1)	1919 (86.9)	1.21 (0.89-1.67)	0.230
Illiterate	462 (17.3)	51 (11.0)	411 (89.0)	1	
Employment					
Employed	1862 (69.7)	239 (12.8)	1623 (87.2)	1.03 (0.80-1.32)	0.811
Unemployed	808 (30.3)	101 (12.5)	707 (87.5)	1	
Marital status					
Not living with partner	1089 (40.8)	141 (12.9)	948 (87.1)	1.03 (0.82-1.30)	0.784
Living with partner	1581 (59.2)	199 (12.6)	1382 (87.4)	1	
CD4 count at ART initiation cells/mm^3					
≤500	2387 (89.4)	318 (13.3)	2069 (86.7)	1.82 (1.16-2.86)	0.009
>500	283 (10.6)	22 (7.8)	261 (92.2)	1	
Past history of TB					
Yes	617 (23.1)	96 (15.6)	521 (84.4)	1.37 (1.06-1.76)	0.017
No	2053 (76.9)	244 (11.9)	1809 (88.1)	1	
ART drug adherence					
≤95	181 (6.8)	34 (18.8)	147 (81.2)	1.65 (1.12-2.44)	0.012
>95	2489 (93.2)	306 (12.3)	2183 (87.7)	1	
ART status					
Non regular (loss to follow-up/opted out)	53 (2.0)	12 (22.6)	41 (77.4)	2.04 (1.06-3.93)	0.032
Regular	2617 (98.0)	328 (12.5)	2289 (87.5)	1	
Duration on ART (years)					
≤1	50 (1.9)	8 (16.0)	42 (84.0)	1.24 (0.57-2.66)	0.590
1.1-3	329 (12.3)	30 (9.1)	299 (90.9)	0.65 (0.44-0.97)	0.034
3.1-5	353 (13.2)	43 (12.2)	310 (87.8)	0.90 (0.64-1.27)	0.546
>5	1938 (72.6)	259 (13.4)	1679 (86.6)	1	-
Regimen at ART initiation					
Others	495 (18.5)	72 (14.5)	423 (85.5)	1.12 (0.83-1.50)	0.461
Tenofovir based	679 (25.4)	70 (10.3)	609 (89.7)	0.75 (0.56-1.01)	0.055
Zidovudine based	1496 (56.0)	198 (13.2)	1298 (86.8)	1	-
ART regimen substitution					
Yes	892 (33.4)	157 (17.6)	735 (82.4)	1.86 (1.48-2.34)	<0.001
No	1778 (66.6)	183 (10.3)	1595 (89.7)	1	

The mean duration of ART treatment was 7.2 year (median 7.2 year, SD:3.3, range 2 months to 15 year, IQR 4.7-9.7 year). Nearly three fourth of the participants (73%; 1938/2670) were taking antiretroviral treatment for more than five years; only 2% (50/2670) PLHIV were on ART for less than or equal to one year. In addition, of the participants who were on ART, 679 (25%) were on tenofovir based regimen and 1496 (56%) were on zidovudine-based regimen at enrolment. Most of the study participants (98%; 2617/2670) were regular for treatment and follow up at the ART centre. Nearly one

third of the PLHIV in the study, (33%; 892/2670) had ART regimen substitution since their treatment initiation due to toxicity, anti-tubercular treatment or change in the National guidelines.

Table 2: Multivariable analysis of association of variables with virological failure among PLHIV.

Exposure variables	Adjusted odds ratio	95% CI of AOR	P value
Age (years)			
≤40	1.91	1.50-2.44	<0.001
>40	Reference		
Gender			
Male	1.52	1.20-1.94	0.001
Female	Reference		
CD4 count at ART initiation cells/mm^3			
≤500	1.71	1.08-2.70	0.022
>500	Reference		
ART drug adherence %			
≤95	1.55	1.04-2.32	0.031
>95	Reference		
ART status			
Non regular (loss to follow-up/opted out)	1.81	0.93-3.55	0.082
Regular	Reference		
ART regimen substitution			
Yes	1.83	1.44-2.33	<0.001
No	Reference		
History of TB			
Yes	1.15	0.88-1.51	0.306
No	Reference		

Ninety three percent (2489/2670) PLHIV had more than 95% drug adherence. Two percent (53/2670) of the PLHIV had opted out of treatment and were loss to follow up. About a fifth of the PLHIV (23%, 617/2670) had history of tuberculosis About a fifth of the PLHIV (23%, 617/2670) had history of tuberculosis. The proportion of virological failure among study participants was 13% (340/2670).

Univariate analysis

Univariate analysis was conducted to study the associations between various attributes of the study participants and virological failure (Table 1). Gender was found to be significantly associated with the outcome of the study (15%, 184/1272; OR 1.35, 95%CI 1.07-1.69; p=0.011). PLHIV less than 40 year of age had greater probability of having virological failure (17%; 139/831) compared to the others (11%; 201/1839). There was no significant association between level of literacy, employment status, ART initiation regimen and duration of antiretroviral therapy with virological failure. PLHIV with CD4 count of ≤500 cells/mm^3 at ART initiation had higher occurrence (13%, 318/2387; OR 1.82, 95% CI 1.16-2.86; p=0.009) of virological failure as compared to others. The prevalence of virological failure was observed to be higher among PLHIV with history of tuberculosis (16%, 96/617) compared to those with no history. Adherence to ART was significantly associated with virological failure and the odds of virological failure was about 1.7 times higher (OR 1.65, 95% CI 1.12-2.44, p=0.012) among PLHIV who had ≤95% drug adherence as compared to others. Of the total 617 study participants having tuberculosis prior to viral load testing, 16% (96/617) had virological failure (OR 1.37, 95% CI 1.06-1.76). Participants with ART substitution had nearly two times higher odds of having virological failure (OR 1.86, 95% CI 1.48-2.34, p<0.001).

Multivariate analysis

The variables included in multivariate model were age, gender, CD4 count at ART initiation, history of tuberculosis, ART drug adherence, status at ART centre and ART substitution (Table 2). Multivariate analysis showed factors associated with the outcome of virological failure. PLHIV with age less than 40 years had significantly higher risk of virological failure as compared to others (adjusted OR 1.91; 95% CI: 1.50-2.44; p<0.001). Men were one and half times more likely to have virological failure as compared to women (adjusted OR 1.52; 95% CI: 1.20-1.94; p=0.001). Those with CD4 count of less than or equal to 500 cells/mm^3 at treatment initiation and ART adherence ≤95% had higher risk for virological failure as compared to others (adjusted OR 1.71; 95% CI 1.08-2.70; p=0.022) and (adjusted OR 1.55, 95% CI of AOR 1.04-2.32; p=0.031) respectively. PLHIV with ART substitution due to

various reasons were almost twice as likely to have virological failure (adjusted OR 1.83, 95% CI 1.44-2.33; p<0.001) compared to their counterparts.

DISCUSSION

Current cross-sectional retrospective study estimated the prevalence and determinants of virological failure among people living with HIV on ART in a public-sector government ART centre. The overall prevalence of virological failure among adults receiving antiretroviral therapy in our study was similar to prior studies with limited sample size from western and southern India.[12] A recent study showed a virological failure of 12% in Mumbai at the beginning of the viral load monitoring, while a suppression of 92% was observed among the subgroup of PLHIV tested for routine monitoring.[7] Developing countries have reported prevalence ranging from 9% to 13% for virological failure among PLHIV accessing antiretroviral therapy.[13-15] This may be attributed to the differences in study design, age groups, duration on ART, drug regimen, treatment adherence, study period and definition of virological failure considered for analysis in all these studies. Higher risk of virological failure was observed among men as compared to women similar to a study from western India and other developing countries though few studies have not reported any association.[7,13,15] The reasons for vulnerability of men to virological failure might be due to less healthcare-seeking behaviours and ART uptake, higher body mass index as compared to women which is more likely to maintain a lower concentration of drugs in their bodies than women, and socio culture habits like smoking and drinking which can lead to poorer adherence to medication and virological suppression.[16-20] PLHIV less than 40 year had significant risk of virological failure as found in southern Indian study and Ethiopian population.[15,19,20] Various behavioural and psychosocial factors like anxiety, stigma, lack of disclosure and low social economic status can be linked to this outcome.[14] Younger age group focusing more on their occupation and earnings can lead to neglected health seeking behaviour especially in asymptomatic individuals.[21,22] Younger age is also associated with poor adherence due to various socio behavioural factors. This strongly highlights focusing on the importance of needs assessment and counselling of younger infected individuals on treatment during their follow up visits to achieve virological suppression. Lower CD4 count at ART initiation was also found to be significantly associated with the outcome, so was seen in studies from other developing countries.[20,23-25]

The findings of the HIV prevention trials network 071 (PopART) trial in South Africa has shown that those initiated on ART with CD4 counts ≥500 cells/µl had good virological outcomes, compared to those with CD4 counts 200–499 cells/µl. The authors mentioned that greater host immune responses, lower baseline VL, fewer co-morbidities, less concomitant medication, and fewer drug-drug interactions were potential mechanisms for improved virological outcomes with baseline CD4 count ≥500 cells/µl.[26] Treat all policy and early linkages to ART centres as per the national programme guidelines assures timely initiation of ART. This helps in targeting the second 90 of UNAIDS goal, thus reducing morbidity and mortality in these individuals. The ART substitutions at ART centres, mainly for drug toxicities, side-effects and drug-drug interactions are decided as per the national ART guidelines.[27] Noticeably, ART substitution was associated with the outcome. In a Nigerian study, ART-related anaemia was found to increase the odds of late virological failure.[28] Many studies showed adverse drug reactions (ADR) to be significantly associated with poor immunologic and virological outcomes among people living with HIV.[29-31] This warrants the routine monitoring for all associated ADR and toxicities for preventing poor virological outcome.

PLHIV experiencing severe ADR were less likely to be ≥90% adherent to ART and may have higher virological failure.[32,33] Poor drug adherence was found to be associated with virological failure in studies from India, Ethiopia and Uganda.[8,20,25,34] Recently published study from Ethiopia also showed that poor ART adherence level was significantly associated with viral non suppression.[15] Detectable viral RNA among PLHIV receiving ART was associated with suboptimal adherence to ART. This is further responsible for the emergence of drug-resistant strains of the virus. One of the important studies conducted in San Francisco using continuous measures for adherence and virological suppression has shown that each 10% decrease in adherence was found to result in a doubling of the viral load. The study suggested that small changes in adherence can result in major differences in virological outcome and that adherence may be the predominant factor determining virological outcomes.[35] Poor adherence was associated variable and unavailability of ART was the single most common cause for incomplete adherence as seen in rural Cameroon, suggesting need to conduct regular and continuous adherence counselling sessions at every ART centre follow-up visit as this encourages PLHIV to discuss barriers to treatment.[36] This is also supported by the recent National operational guidelines for viral load testing.[3] Regular viral load monitoring integrated with intensive adherence counselling sessions has improved the drug adherence among PLHIV resulting in prevention of switch to second line ART regimen.[37,38] Therefore, adherence counseling must be done before repeat VL testing to avoid ART switch to second line regimen in the programme, especially among those living without partners.[9] In decentralized clinics, reporting test results on the same-day and shorter time-to switch ART regimen had proven the potential of point of care based VL-testing.[39] Regular staff training, continuous monitoring and creating demand are essential to the success of routine VL testing. Thus, analysis of the data from different parts of the countries suggested that data on

predictors of treatment failure will help in achieving and understanding last 90 target of virological suppression.[2]

Current paper describes data from a public-sector government ART centre which attempts to assess the virological failure among PLHIV on treatment after the launch of the NACO viral load testing guidelines for programme monitoring in 2018. We report findings from a single ART centre which has its own limitations. As with all cross-sectional studies, causal inferences about the associations could not be unfolded. Data on death and transferred out PLHIV at the ART centre were not included which might have underestimated the outcome and transferred out PLHIV at the ART centre were not included which might have underestimated the outcome. As per the national guidelines, the study involved analysis based on a single viral load assay; hence may not reveal accurate treatment failure.

CONCLUSION

The present investigation has highlighted some important aspects for programmatic consideration. The study demonstrated that virological failure was associated with factors amenable to recognition through regular screening and early interventions. Younger age, gender, low baseline CD4 count at ART initiation and poor ART drug adherence were significant determinants of virological failure. Early linkage to treatment and ART initiation along with adherence counselling at every follow up visit play an important role in mitigating virological failure. Individuals with treatment switches need additional counselling sessions and adherence monitoring to achieve virological suppression which subsequently reduces drug resistance. Newer management strategies integrated with the existing HIV programme, continuing follow-up patient centric care can help in leveraging existing early detection and management of virological failure among people living with HIV.

ACKNOWLEDGEMENTS

The authors acknowledge the support of care, support and treatment (CST) division of National AIDS Control Programme, CST officials at the Maharashtra State AIDS Control Society, and staff of NARI ART centre. Authors would like to thank ICMR-National AIDS Research Institute for supporting the study. The study team gratefully acknowledges the support from staff of Virology Division of ICMR-NARI and Metropolis healthcare for performing viral load testing.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. National AIIDS control organization, Ministry of health and family welfare, Government of India, Annual report 2017-18. Available at: http://naco.gov.in/sites/default/files/Annual Report NACO-2017-18 %281%29.pdf. Accessed on 20 January 2021
2. Joint United Nations programme on HIV/AIDS (UNAIDS), an ambitious treatment target to help end the AIDS epidemic. Available at: http://www.unaids.org/en/resources/documents/2017/90-90-90. Accessed on 20 January 2021.
3. National operational guidelines for viral load testing, Ministry of health and family welfare, Government of India. Available at: http://www.naco.gov.in/sites/default/files/National %20Operational%20Guidelines%20for%20Viral%20Load%20Testing%20Mar%2718.pdf. Accessed on 20 January 2021.
4. Habiyambere V, Dongmo Nguimfack B, Vojnov L, Ford N, Stover J, Hasek L, et al. Forecasting the global demand for HIV monitoring and diagnostic tests: A 2016-2021 analysis. PLoS One. 2018;13(9): e0201341.
5. Mungwira RG, Divala TH, Nyirenda OM, Kanjala M, Muwalo F, Mkandawire FA, et al. A targeted approach for routine viral load monitoring in Malawian adults on antiretroviral therapy. Trop Med Int Health. 2018;23(5):526-32.
6. Chadha S, Bhalla P, Jha AK, Gautam H, Saini S, Anuradha S, et al. Disease progression and antiretroviral therapy in newly seropositive HIV subjects in a tertiary care hospital in North India. J Infect Dev Ctries. 2013;7(2):54-9.
7. Laxmeshwar C, Acharya S, Das M, Keskar P, Pazare A, Ingole N, et al. Routine viral load monitoring and enhanced adherence counselling at a public ART centre in Mumbai, India. PLoS One. 2020;15(5): e0232576.
8. Karade SK, Ghate M V, Chaturbhuj DN, Kadam DB, Shankar S, Gaikwad N, et al. Cross-sectional study of virological failure and multinucleoside reverse transcriptase inhibitor resistance at 12 months of antiretroviral therapy in Western India. Medicine. 2016;95(37):e4886.
9. Shet A, Neogi U, Kumarasamy N, DeCosta A, Shastri S, Rewari BB. Virological efficacy with first-line antiretroviral treatment in India: predictors of viral failure and evidence of viral resuppression. Trop Med Int Health. 2015;20(11):1462-72.
10. National guidelines for HIV-1 viral load laboratory testing, Ministry of Health and Family Welfare, Government of India. Available at: http://www.naco. gov.in/sites/default/files/National GuidelinesForHIV-1ViralLoadLaboratoryTesting April2018%20%282%29.pdf. Accessed on 20 January 2021.
11. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing hiv infection: recommendations for a public health approach. Available at: https://apps.who.int/iris/handle/10665/208825. Accessed on 20 January 2021.

12. Hingankar NK, Thorat SR, Deshpande A, Rajasekaran S, Chandrasekar C, Kumar S, et al. Initial virologic response and HIV drug resistance among HIV-infected individuals initiating first-line antiretroviral therapy at 2 clinics in Chennai and Mumbai, India. Clin Infect Dis. 2012;54(4):S348-54.
13. Ojha CR, Shakya G, Dumre SP. Virological and immunological status of the people living with HIV/AIDS undergoing ART treatment in Nepal. Biomed Res Int. 2016;2016:6817325.
14. Kiweewa F, Esber A, Musingye E, Reed D, Crowell TA, Cham F, et al. HIV virologic failure and its predictors among HIV-infected adults on antiretroviral therapy in the African Cohort Study. PLoS One. 2019;14(2):e0211344.
15. Desta AA, Woldearegay TW, Futwi N, Gebrehiwot GT, Gebru GG, Berhe AA, et al. HIV virological non-suppression and factors associated with non-suppression among adolescents and adults on antiretroviral therapy in northern Ethiopia: a retrospective study. BMC Infect Dis. 2020;20(1):4.
16. Tran DA, Wilson DP, Shakeshaft A, Ngo AD, Doran C, Zhang L. Determinants of virological failure after 1 year's antiretroviral therapy in Vietnamese people with HIV: findings from a retrospective cohort of 13 outpatient clinics in six provinces. Sex Transm Infect. 2014;90(7):538-44.
17. Jordan MR, Obeng-Aduasare Y, Sheehan H, Hong SY, Terrin N, Duong D V, et al. Correlates of non-adherence to antiretroviral therapy in a cohort of HIV-positive drug users receiving antiretroviral therapy in Hanoi, Vietnam. Int J STD AIDS. 2014;25(9):662-8.
18. Cauldbeck MB, O'Connor C, O'Connor MB, Saunders JA, Rao B, Mallesh VG, et al. Adherence to anti-retroviral therapy among HIV patients in Bangalore, India. AIDS Res Ther. 2009;6:7.
19. Meshesha HM, Nigussie ZM, Asrat A, Mulatu K. Determinants of virological failure among adults on first-line highly active antiretroviral therapy at public health facilities in Kombolcha town, Northeast, Ethiopia: a case–control study. BMJ Open. 2020; 10(7):e036223.
20. Bayu B, Tariku A, Bulti AB, Habitu YA, Derso T, Teshome DF. Determinants of virological failure among patients on highly active antiretroviral therapy in University of Gondar Referral Hospital, Northwest Ethiopia: a case-control study. HIV AIDS. 2017;9: 153-9.
21. Kim S-H, Gerver SM, Fidler S, Ward H. Adherence to antiretroviral therapy in adolescents living with HIV: systematic review and meta-analysis. AIDS. 2014;28(13):1945-56.
22. Semvua SK, Orrell C, Mmbaga BT, Semvua HH, Bartlett JA, Boulle AA. Predictors of non-adherence to antiretroviral therapy among HIV infected patients in northern Tanzania. PLoS One. 2017;12(12): e0189460.
23. Kyaw NTT, Harries AD, Kumar AM V, Oo MM, Kyaw KWY, Win T, et al. High rate of virological failure and low rate of switching to second-line treatment among adolescents and adults living with HIV on first-line ART in Myanmar, 2005-2015. PLoS One. 2017;12(2):e0171780.
24. Datay MI, Boulle A, Mant D, Yudkin P. Associations with virologic treatment failure in adults on antiretroviral therapy in South Africa. J Acquir Immune Defic Syndr. 2010;54(5):489-95.
25. Ahmed M, Merga H, Jarso H. Predictors of virological treatment failure among adult HIV patients on first-line antiretroviral therapy in Woldia and Dessie hospitals, Northeast Ethiopia: a case-control study. BMC Infect Dis. 2019;19(1):305.
26. Fatti G, Grimwood A, Nachega JB, Nelson JA, LaSorda K, van Zyl G, et al. Better Virological Outcomes Among People Living With Human Immunodeficiency Virus (HIV) Initiating Early Antiretroviral Treatment (CD4 Counts ≥500 Cells/μL) in the HIV Prevention Trials Network 071 (PopART) Trial in South Africa. Clin Infect Dis an Off Publ Infect Dis Soc Am. 2020;70(3):395-403.
27. National technical guidelines on anti retroval treatment. Available at: www.naco.gov.in. Accessed on 20 January 2021.
28. Abah IO, Ncube NBQ, Bradley HA, AgbaJi OO, Kanki P. Antiretroviral therapy-associated adverse drug reactions and their effects on virologic failure-A retrospective Cohort Study in Nigeria. Curr HIV Res. 2018;16(6):436-46.
29. Syed IA, Sulaiman SAS, Hassali MA, Syed SH, Shan LH, Lee CKC. Factors associated with poor CD4 and viral load outcomes in patients with HIV/AIDS. J Med Virol. 2016 May;88(5):790-7.
30. Njuguna C, Orrell C, Kaplan R, Bekker L-G, Wood R, Lawn SD. Rates of switching antiretroviral drugs in a primary care service in South Africa before and after introduction of tenofovir. PLoS One. 2013; 8(5):e63596.
31. Bezabhe WM, Bereznicki LR, Chalmers L, Gee P, Kassie DM, Bimirew MA, et al. Adverse drug reactions and clinical outcomes in patients initiated on antiretroviral therapy: a prospective cohort study from ethiopia. Drug Saf. 2015;38(7):629-39.
32. Cardoso SW, Grinsztejn B, Velasque L, Veloso VG, Luz PM, Friedman RK, et al. Incidence of modifying or discontinuing first HAART regimen and its determinants in a cohort of HIV-infected patients from Rio de Janeiro, Brazil. AIDS Res Hum Retroviruses. 2010;26(8):865-74.
33. Shubber Z, Calmy A, Andrieux-Meyer I, Vitoria M, Renaud-Théry F, Shaffer N, et al. Adverse events associated with nevirapine and efavirenz-based first-line antiretroviral therapy: a systematic review and meta-analysis. AIDS. 2013;27(9):1403-12.
34. Ahoua L, Guenther G, Pinoges L, Anguzu P, Chaix M-L, Le Tiec C, et al. Risk factors for virological failure and subtherapeutic antiretroviral drug concentrations in HIV-positive adults treated in rural northwestern Uganda. BMC Infect Dis.

2009;9:81.
35. Bangsberg DR, Hecht FM, Charlebois ED, Zolopa AR, Holodniy M, Sheiner L, et al. Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. AIDS. 2000;14(4):357-66.
36. Zoufaly A, Jochum J, Hammerl R, Nassimi N, Raymond Y, Burchard GD, et al. Virological failure after 1 year of first-line ART is not associated with HIV minority drug resistance in rural Cameroon . J Antimicrob Chemother. 2015;70(3):922-5.
37. Jobanputra K, Parker LA, Azih C, Okello V, Maphalala G, Jouquet G, et al. Impact and programmatic implications of routine viral load monitoring in Swaziland. J Acquir Immune Defic Syndr. 2014;67(1):45-51.
38. Sigaloff KCE, Hamers RL, Wallis CL, Kityo C, Siwale M, Ive P, et al. Unnecessary antiretroviral treatment switches and accumulation of HIV resistance mutations; two arguments for viral load monitoring in Africa. J Acquir Immune Defic Syndr. 2011;58(1):23-31.
39. Nicholas S, Poulet E, Wolters L, Wapling J, Rakesh A, Amoros I, et al. Point-of-care viral load monitoring: outcomes from a decentralized HIV programme in Malawi. J Int AIDS Soc. 2019;22(8): e25387.

Cite this article as: Shidhaye P, Lokhande N, Kulkarni S, Gurav S, Deoraj P, Ghate M. Virological failure among HIV infected individuals on antiretroviral therapy in Pune, India: a cross-sectional study. Int J Adv Med 2021;8:1193-200.