

Is tenofovir-based ART regimen challenging the survival of people living with HIV/AIDS attending a rural-based ART center of eastern India? A retrospective cohort study

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Abstract

Introduction: This research was conducted to assess the predictors for poor survival of patients living with human immunodeficiency virus (HIV) in a rural-based setting.

Material and methods: In this retrospective cohort study, 92 HIV-positive individuals were selected by a simple random sampling method out of a total of 853 patients, who registered at the anti-retroviral therapy (ART) clinic of Bankura Sammilani Medical College and Hospital before January 1, 2017. Selected participants were followed up until December 31, 2021, or until death, through reviewing secondary data, such as the ART enrolment register and the death register. Patients with incomplete data or who were transferred to other ART centers were excluded. Survival probability was expressed using life table and Kaplan-Meier plots. In bivariate analysis, statistically significant variables ($p < 0.05$) were considered for Cox regression model, from which, hazard ratio was assessed.

Results: The overall HIV death incidence density rate from diagnosis until last observation was 2.65 per 100 person-years. In the last 5 years, the rate increased to 4.49 per 100 person-years. At the end of 5-year follow-up period, the cumulative survival probability was 79%. However, it is of concern that in the last year of follow-up, the survival probability drastically decreased from 90% to 79%. Patients who received TLE [tenofovir (TDF) + lamivudine (3TC) + efavirenz (EFV)] regimen for a maximum duration were found 2.83 times more vulnerable to death (hazard ratio = 2.830; 95% CI: 1.538-5.209%).

Conclusions: Investigating the TLE regimen's risk assessment is crucial for patient safety and better health outcomes.

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Key words: survival probability, TLE regimen, life table, Kaplan-Meier plot, Cox regression model.

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Introduction

Since 1980, acquired immuno-deficiency syndrome (AIDS) started to emerge as the epidemic. According to UNAIDS Global HIV & AIDS statistics – 2020 fact sheet, 77.5 million people have been affected by this disease and 34.7 million died from HIV/AIDS-related causes since the start of the epidemic. As per the same report, globally, 37.6 million people were living with human immunodeficiency virus (HIV) in 2020, and only 84% of them knew their HIV status [1]. In this long journey of the epidemic, AIDS-related deaths have decreased by 61% since 2004 after successful implementation of anti-retroviral therapy (ART) [2]. Introduction of ART drastically reduced the mortality rate of HIV patients and improved their overall quality of life [3]. As per NACO – 2021 HIV fact sheet, 2,349,000 people were living with HIV in India in 2019 [4].

A meta-analysis conducted on 57 studies compared the survival probability of AIDS-diagnosed patients according to their highly active antiretroviral therapy (HAART) status. The authors observed that declining of survival probability among non-receivers of HAART was higher (48%, 26%, and 18% on 2nd, 4th and 6th year of follow-up, respectively) compared with HAART receivers (87%, 86%, and 78% on 2nd, 4th and 6th year of follow-up, respectively) [5]. The effectiveness of ART varies from country to country [6, 7]. However, majority of previous studies showed that the rate of disease progression from HIV to death was significantly reduced by ART, but discrepancy in survival rates of HIV-infected people was also reported in some studies [8, 9]. Decline in the incidence and mortality rate throughout the globe after widespread ART utilization, is not uniform for all countries.

The survival of patients depends on various factors. In a study done in Kombolcha, the survival was better among participants aged 18-29 years in comparison with those aged 60 years or more. Survival time of patients from urban settings was better than that of rural residents. Moreover, the survival time was less in participants who did not attend any education than those with primary education. Participants with body weight of 60 kg or more had better survival time than those with weight less than 60 kg. Similarly, HIV individuals with CD4+ count of 350 or more were surviving better versus patients with CD4+ count less than 50. Participants with good adherence to medications lived better than those with poor adherence, whereas those with opportunistic infections survived less in comparison with their coun-

terparts [10]. In a study from Ethiopia, an association was found among the risk of mortality of HIV-tuberculosis (TB) co-infected children with treatment failure, CD4+ count below the threshold level, and non-users of cotrimoxazole preventive therapy (CPT) [11].

Adherence to ART critically affects HIV-1 RNA viral suppression [12-14]. A study from Jharkhand reported that good adherence increases the chance of survival among people living with HIV/AIDS (PLWHA) [15].

Despite the initiation and successful implementation of ART as well as good adherence to ART, survival probability of HIV patients is not satisfactory due to several hidden predictors. From public health perspective, this is an important gap in the literature. On this background, the present research was conducted to assess the predictors of poor survival of HIV patients in a rural-based setting, where there was lack of information in this regard. These findings may provide valuable insights into the health outcomes of PLWHA, and can help support interventions to improve quality of life and lifespan of HIV-infected patients.

Material and methods

This retrospective cohort study was conducted at a rural-based ART center of eastern India, situated in a tertiary care hospital of West Bengal, Bankura Sammilani Medical College and Hospital. The center was open in 2015, and till date serving HIV-infected people from districts, such as Bankura, Purulia, Paschim Bardhaman, etc. At the time of study, 1,402 patients were registered in this center and 1,273 of them were attending the center for regular follow-up visits. The center is run by one medical officer, one institutional staff nurse, one counsellor/data manager, and one counsellor/pharmacist.

The study was conducted between May 18, 2022 and July 17, 2022. All patients registered at the ART clinic of Bankura Sammilani Medical College and Hospital before January 1, 2017 were considered the study cohort. Patients, whose follow-up data were incomplete in the register and who have been transferred to other ART centers, were excluded. The study was initiated by comparing multiple possible exposure factors with their corresponding non-exposed factors, which were assessed through the records on January 1, 2017. Patients outcomes were compared at the end of every follow-up's year and at the end of 5 years, all from the same secondary data source. An outcome of the study was assessed in terms of "Alive" or "Dead" only (Figure 1).

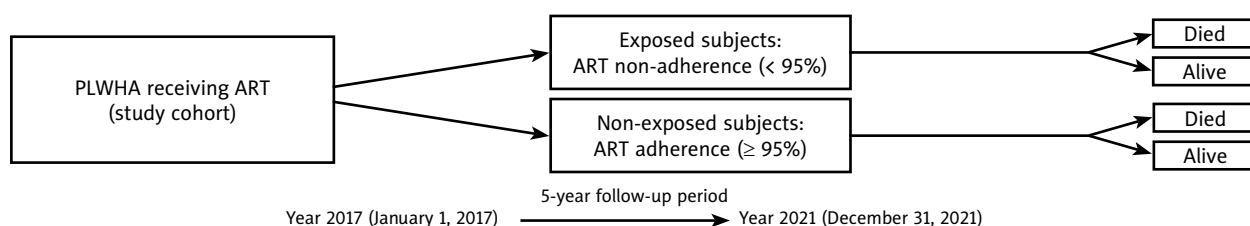


Figure 1. Schematic diagram of the retrospective cohort study

Sample size for the exposed group was calculated by using the following formula:

$$n = \frac{\left[Z_{\alpha} \sqrt{\left(1 + \frac{1}{m}\right) p^* (1 - p^*)} + Z_{\beta} \sqrt{p_1 \frac{(1 - p_1)}{m}} + p_2 (1 - p_2) \right]}{(p_1 - p_2)^2}$$

where $Z_{\alpha} = 1.96$, $Z_{\beta} = 0.84$, p_1 is the probability of death in PLWHA with WHO stage 3/4 = 0.28, p_2 is the probability of death in PLWHA with WHO stage 1/2 = 0.08, $p^* = 0.18$, and $m = 1$ (equal number of exposed and non-exposed persons assumed). Using the above formula, sample size for the exposed group was 46. Therefore, the calculated total sample size was $2 \times 46 = 92$. Before 2017, a total 853 patients were registered in the center and were receiving ART; hence, these 853 patients were considered as the sampling frame. From this sampling frame, 92 patients were selected by using a simple random sampling method with computer-generated random numbers.

After obtaining necessary permission from the Institutional Ethics Committee (IEC; approval number: BSMC/IEC: 847, dated April 5, 2022) and medical officer in charge of the ART center, data collection was started. Data were collected by reviewing ART enrolment register and death register (secondary data source) of the ART center using pre-designed questionnaire proforma for reviewing records. From these secondary data source, patients' outcomes were investigated from January 1, 2017 to December 31, 2021, or till death. Data related to socio-demographic and clinical profile, treatment history, follow-up, and outcomes of all registered patients were maintained meticulously by a designated person. Patient's profile and clinical condition were updated timely according to National AIDS Control Programme (NACP), which could be considered as a good quality secondary data for a follow-up research. In this study, participants were followed up as per their ID numbers, whereas their anonymity and confidentiality were maintained throughout the study.

In the present research, PLWHA who used $\geq 95\%$ of total monthly dose of ART medication were considered as ART adherent, while HIV patients, whose names were registered in HIV death register as "Dead", were considered as HIV-related death. If the gap between date of eligibility of ART initiation and ART starting date was more than 2 months, it was considered as delayed ART initiation.

Data were entered in Microsoft Excel worksheet (Microsoft, Redwoods, WA, USA), and analyzed using IBM Statistical Package for the Social Sciences software, version 16.0 (SPSS Inc., Chicago, IL, USA) and Microsoft Excel. Incidence of HIV death density rate (IDR) was defined as the number of deaths due to HIV occurring per 100 patient-years of observation. The incidence of HIV death density rate was measured at the end of every year. Survival period was stratified by baseline immunological and clinical profile, and compared using Mann-Whitney U test or Kruskal-Wallis test, as per applicability. Survival probability was expressed by life table and Kaplan-Meier plots. Survival of HIV patients was defined as the time of enrolment till the date of death due

to HIV. Statistically significant variables ($p < 0.05$) in bivariate analysis were considered for Cox regression model, from which, hazard ratio was assessed.

The current study was conducted under the authority of the ICMR (Indian Council of Medical Research) – Short Term Studentship (STS) 2022 Program (STS reference ID: 2022-05791).

Results

The median age of 92 study subjects was 30 years (interquartile range, IQR: 16). The majority of study participants were males (59.7%), Hindu (93%), having low socioeconomic status (81.5%), and resided in rural area (75%). Most of the patients were married (86.1%) and home-makers (33.7%). One-fourth of them were illiterate (25%), and 18.6% and 15.2% were scheduled tribe and scheduled caste, respectively. Fifty to seventy-four percent of family members of one-fifth study subjects (21.7%) were HIV-positive. Nearly half (44.6%) of the study population were substance abusers, and 26.1% were suffering from co-morbidities. Majority of them (54.2%) had extra-pulmonary tuberculosis as co-morbidity. The most common mode of infection was through heterosexual contact (78.3%), followed by blood transfusion (9.8%), mother-to-child transmission (4.3%), MSM (4.3%), and unknown (3.3%). The majority of study participants' (55.4%) baseline WHO staging was I, followed by stage II (20.6%) and IV (17.5%). Within 5-year observation per subject, the average 46.2 months was considered stage I, and it was the highest time considered when compared with other stages. About one-fourth of the persons (28.3%) had a history of receiving CPT, while only 0.75% per 100 person-years observation had a history of opportunistic infection.

Regarding ART, one-third (33.7%) of the study subjects initiated ART in delay (more than 2 months). TLE [tenofovir (TDF) + lamivudine (3TC) + efavirenz (EFV)] combination was the most commonly (52.2%) used regimen among the patients, followed by ZLN [zidovudine (AZT) + lamivudine (3TC) + nevirapine (NVP)] (31.5%) and ZLE [zidovudine (AZT) + lamivudine (3TC) + efavirenz (EFV)] (15.2%) regimens. Only 2.2% of the study subjects had a history of ART discontinuation during the follow-up period, while only 40.2% of the participants were found to be fully adherent to ART. Majority of the patients (66.3%) had CD4+ count between 200-499 cells/cmm, 26.1% had CD4+ count below 200 cells/cm², and only 7.6% had CD4+ count above 500 cells/cm².

The total observation time was 716.11 person-years, and in the 5 years of observation period was 423.26 person-years. After diagnosis of HIV till last observation, the overall HIV death incidence density rate was 2.65 per 100 person-years, and in the 5 years of observation period, HIV death incidence density rate was 4.49 per 100 person-years. At the end of follow-up period, the 5-year cumulative survival probability was 79%. In the last year of follow-up period, the sur-

Table 1. Life table for 5-year survival analysis of HIV-positive patients ($n = 92$)

Interval start time	Number of entering interval	Number of withdrawing during interval	Number of exposed to risk	Number of terminal events	Proportion terminating	Proportion surviving	Cumulative proportion surviving at end of interval	Number of person-years observation of risk population	Incidence of death per 100 person-years
0	92	0	92.000	1	0.01	0.99	0.99	91.05	1.10
1	91	0	91.000	3	0.03	0.97	0.96	88.75	3.38
2	88	0	88.000	2	0.02	0.98	0.93	85.75	2.33
3	86	1	85.500	3	0.04	0.96	0.90	80.91	3.71
4	82	2	81.000	10	0.12	0.88	0.79	76.81	13.02

vival probability rate drastically decreased: from 90% to 79% (Table 1).

In the bivariate analysis, baseline WHO stage III, using TLE regimen for maximum duration, poor ART adherence, and history of ART discontinuation, were found significantly related to higher incidence density rate of death (Table 2).

Factors, which were found statistically significant in bivariate analysis, were considered for Cox regression model. Before considering for Cox regression model, variables were recoded as 1 or 0. Factors related to a higher incidence density rate of death were coded as 1, and the rest as 0. In this model, death was coded as 1.

Ultimately, ART regimen was found statistically significant in Cox regression analysis. Patients who received TLE regimen for maximum duration were found 2.83 times more vulnerable to death: hazard ratio = 2.830; 95% CI: 1.538-5.209% (Table 3). Kaplan-Meier plot demonstrated that PLWHA who were on TLE regimen had poor survival than those on other regimens. Log-rank test (Mantel-Cox) ($\chi^2 = 9.123$, $df = 3$, $p = 0.03$) indicated that observation was statistically significant (Figure 2).

Discussion

This retrospective cohort study investigated data of registered patients from the ART clinic of Bankura Sammilani Medical College and Hospital. The study cohort comprised PLWHA who registered before January 1, 2017, and were followed up till December 31, 2021 from secondary data sources. The study assessed the survival probability of patients, described their socio-demographic and baseline clinical profiles, and searched for predictors of mortality or poor survivability. During the total observation period of 716.11 person-years, the observation period of 5 years was 423.26 person-years. The median age of the study subjects was 30 years, with an interquartile range of 16. It is interesting to note that the mean age of people living with HIV/AIDS

in other studies conducted in India varied from 32.77 in the Jain study [16] to 39.5 years in the Tamil Nadu [17] and the mean age of HIV-infected people was 38.4 years in 2005 in India [18]. In accordance with previous research, it was observed that there was a higher prevalence of males and married individuals. This was noted in both previous studies and the current one [16-18].

It seems that in India, the most common way of spreading the virus is through heterosexual contact. The proportion of cases resulting from this mode of transmission is higher (87%) compared with that found in the present study (78.3%) [19].

According to a recent Ethiopian study, the overall incidence rate of opportunistic infections was found to be 8.97 cases per 100 person-years observation, which is higher than that in the current study (0.75% per 100 person-years observation).

The present study noticed that TLE (52.2%) combination was the most commonly used regimen among the study subjects, followed by ZLN (31.5%) and ZLE (15.2%). Jain *et al.* [16] also found TLE to be the preferred first-line regimen, with a high proportion of choice (85%).

Furthermore, only 40.2% of the study subjects were fully adhered to ART. According to a systematic review and meta-analysis by Akbari *et al.* [20], the adherence rate in India was actually higher, at around 70% (with a 95% CI: 59-81%; $I^2 = 96.3\%$), compared with the present study.

After diagnosis of HIV till last observation, the overall HIV death incidence density rate was 2.65 per 100 person-years, and in the last 5 years, the HIV death incidence density rate was 4.49 per 100 person-years. At the end of follow-up period, the 5-year cumulative survival probability was 79%. In the last year of follow-up, the survival probability drastically reduced: from 90% to 79%.

Based on the findings of Akbari *et al.* [20], it appears that certain factors, such as being male, having a CD4+ count of less than 500 cells/cm³, not receiving ART treat-

Table 2. Bivariate analysis showing the association between variables and HIV death incidence density rate per 100 person-years ($n = 92$)

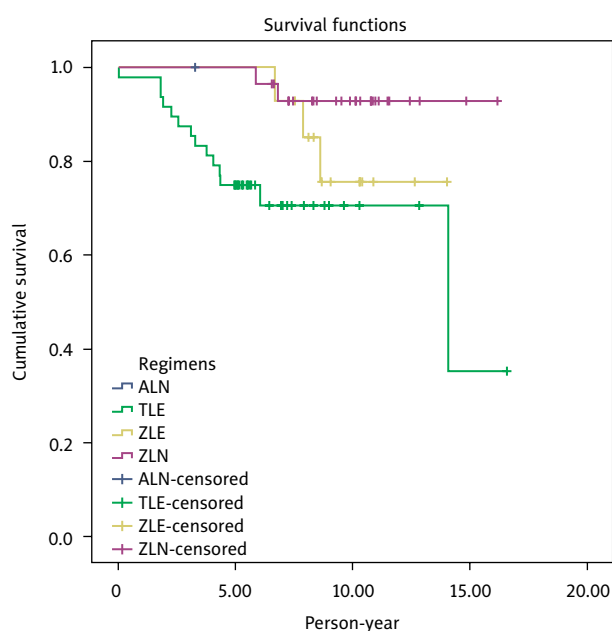
Variables	Number of patients	Total follow-up person-years from the date of registration	Number of cases who died during follow-up period	HIV death incidence density rate per 100 person-years	Test of significance
Age (years)					
< 10	8	61.25	2	3.27	Kruskal-Wallis test: $\chi^2 = 3.804$, df = 4, $p = 0.433$
10-19	6	35.22	3	8.52	
20-29	31	259.85	4	1.54	
30-39	28	222.29	5	2.25	
≥ 40	19	137.50	5	3.64	
Gender					
Male	55	418.33	13	3.10	Kruskal-Wallis test: $\chi^2 = 0.361$, df = 2, $p = 0.835$
Female	36	288.80	6	2.10	
Transgender	1	8.98	0	0	
Religion					
Hindu	86	673.25	17	2.50	Mann-Whitney U test: 223.000, $p = 0.580$
Muslim	6	42.86	2	4.70	
Caste					
General	54	434.34	9	2.10	Kruskal-Wallis test: $\chi^2 = 1.986$, df = 3, $p = 0.575$
OBC	7	48.47	3	6.19	
SC	14	109.96	4	3.64	
ST	17	123.34	3	2.43	
Marital status ($n = 79$)					
Married	68	529.28	14	2.65	Kruskal-Wallis test: $\chi^2 = 2.271$, df = 2, $p = 0.321$
Unmarried	4	26.86	0	0	
Widow(er)	7	69.12	0	0	
Education level ($n = 88$)					
Illiterate	22	171.41	6	3.29	Kruskal-Wallis test: $\chi^2 = 1.874$, df = 2, $p = 0.392$
Primary	35	285.73	7	2.40	
Secondary and above	31	228.59	6	2.62	
SES					
I, II, III	5	33.34	0	0	Kruskal-Wallis test: $\chi^2 = 1.068$, df = 2, $p = 0.586$
IV	12	90.09	3	3.33	
V	75	592.68	16	2.70	
Residence					
Rural	69	526.03	15	2.85	Mann-Whitney U test: 701.500, $p = 0.407$
Urban	23	190.08	4	2.10	
Addiction					
Yes	41	324.51	7	2.16	Mann-Whitney U test: 965.000, $p = 0.527$
No	51	391.60	12	3.06	

Table 2. Cont.

Variables	Number of patients	Total follow-up person-years from the date of registration	Number of cases who died during follow-up period	HIV death incidence density rate per 100 person-years	Test of significance
Co-morbidity					
Yes	24	187.13	5	2.67	Mann-Whitney <i>U</i> test: 779.000, <i>p</i> = 0.742
No	68	528.98	14	2.65	
Mode of infection					
Heterosexual	72	575.84	12	2.08	Kruskal-Wallis test: χ^2 = 4.121, df = 4, <i>p</i> = 0.390
MSM	4	24.29	1	4.12	
Blood transfusion	9	55.21	5	9.06	
Mother-to-child	4	35.64	0	0	
Unknown	3	25.13	1	3.98	
Baseline WHO staging					
I	51	387.99	9	2.32	Kruskal-Wallis test: χ^2 = 14.011, df = 3, <i>p</i> = 0.003
II	19	167.72	4	2.38	
III	6	19.79	4	20.21	
IV	16	140.61	2	1.42	
Opportunistic infection					
Yes	5	44.93	2	4.45	Mann-Whitney <i>U</i> test: 168.500, <i>p</i> = 0.399
No	87	671.18	17	2.53	
ART delay					
Yes	31	262.01	8	3.05	Mann-Whitney <i>U</i> test: 812.500, <i>p</i> = 0.272
No	61	454.10	11	2.42	
ART regimen					
ALN	1	3.28	0	0	Kruskal-Wallis test: χ^2 = 39.173, df = 3, <i>p</i> = 0.000
TLE	48	288.14	14	4.86	
ZLE	14	133.50	3	2.25	
ZLN	29	291.19	2	0.69	
ART discontinuation					
Yes	2	5.67	2	35.27	Mann-Whitney <i>U</i> test: 10.000, <i>p</i> = 0.017
No	90	710.44	17	2.39	
Baseline CD4+ count					
< 200 cells/ cmm	24	185.37	10	5.39	Kruskal-Wallis test: χ^2 = 0.306, df = 2, <i>p</i> = 0.858
200-499 cells/ cmm	61	482.03	8	1.66	
≥ 500 cells/ cmm	7	48.71	1	2.05	
ART adherence					
Yes	37	323.44	5	1.55	Mann-Whitney <i>U</i> test: 661.000, <i>p</i> = 0.005
No	55	392.67	14	3.57	
Chemo-prophylactic treatment received					
Yes	26	206.31	6	2.91	Mann-Whitney <i>U</i> test: 903.000, <i>p</i> = 0.844
No	66	509.80	13	2.55	

Table 3. Beta coefficients in Cox regression model

Variables	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp (B)	
							Lower	Upper
WHO staging (III = 1, rest = 0)	-1.349	0.785	2.953	1	0.086	0.259	0.056	1.209
ART regimen (TLE = 1, rest = 0)	1.040	0.311	11.171	1	0.001	2.830	1.538	5.209
ART discontinuation (Yes = 1, No = 0)	1.350	1.074	1.581	1	0.209	3.856	0.470	31.624
ART adherence (No = 1, Yes = 0)	0.227	0.597	0.145	1	0.703	1.255	0.390	4.042

**Figure 2.** Kaplan-Meier plot showing the cumulative survival probability of PLWHA according to received ART regimens

ment, having HIV-TB co-infection, and being infected through mother-to-child transmission, can increase the risk of mortality. The study also found that the survival probability decreased from 88% to 77% within 5 years. These results underscore the importance of early diagnosis, prompt treatment, and effective management of HIV and its associated conditions.

A study by Mohammadi *et al.* [21] reported that a CD4+ count of less than 200 cells/mm³, tuberculosis co-infection, and lack of ART treatment, can increase the risk of mortality for individuals with HIV. The study also found that the survival probability decreased from 90% to 74% in just five years.

A research of Manosuthi *et al.* [22] shown that having a history of ART switching, major opportunistic infections during ART, baseline CD4+ count ≤ 200 , age ≥ 50 , and receiving nevirapine-based regimens, could increase the risk of mortality for individuals with HIV. In fact, the study demonstrated that the survival probability decreased from 88.2% to 75.1% within five years.

According to a recent study by Moradi *et al.* [23], divorced or isolated HIV-positive individuals, with a low edu-

cation level, unemployed, not under ART, or having a co-infection of HIV and tuberculosis, may present an increased risk of mortality. The study also revealed that the survival probability decreased from 94% to 78% within five years.

A study by Siraj *et al.* [9] reported that poor drug adherence, CD4+ count of less than 100 cells/cmm, being bed-ridden, having opportunistic infections, weighing less than 60 kg, and being WHO stage III or IV, can increase the risk of mortality for persons with HIV, and also observed that the survival probability on the fifth year was 83%.

The mortality risk factors among HIV-infected individuals can vary depending on a study, but a smaller level of CD4+ count, not receiving ART, and HIV-TB co-infection, were commonly reported in various research [10, 21-24]. The present study found that receiving TLE regimen was the only predictor of HIV mortality.

After conducting an extensive literature search, it was found that there is no direct supportive literature about receiving TLE as a predictor of HIV mortality. However, a study by Manosuthi *et al.* [22] reported nevirapine-based therapy as a predictor of HIV mortality. Currently, the TLE regimen is preferred over ZLN and ZLE combinations, based on studies, such as by Badii *et al.* [24], who found that tenofovir-based ART regimen (TLE) responded better in CD4+ count change compared with zidovudine-based ART (ZLE).

Based on a research conducted by Singla *et al.* [25] and Bansal *et al.* [26], it appears that there may be conflicting results regarding the effectiveness of TLE and ZLN regimens in improving the immunological status of HIV-positive patients. While some studies found them to be equally effective, others showed TLE to be more effective. Nonetheless, it is important to note that these studies indirectly oppose the findings of the previous study by Manosuthi *et al.* [22], who reported nevirapine-based therapy as a predictor of HIV mortality.

According to a recent research conducted in Nigeria, dolutegravir-based regimen (TLD) may be more effective than TLE in reducing viral load in HIV-positive patients due to its faster action [28, 29]. The study found that TLD is better tolerated than TLE [30].

The present study raised concerns about the mortality risk associated with TLE; however, no significant side effects were reported. Newer research support the use of TLD or other preferred drugs over TLE, and these are indirectly supporting switching over the preferred drug, from TLE to TLD or better one.

From the healthcare provider's point of view, it is crucial to stay up-to-date with the latest research, and make informed decisions about HIV treatment options for HIV patients. It can be particularly challenging when the ART regimen itself becomes a concern for their survival. We must constantly strive to provide the best possible care and support to those living with HIV.

Conclusions

The study found that the overall HIV death incidence density rate was 2.65 per 100 person-years, while in the last five years, it was 4.49 per 100 person-years. Despite the low mortality rate observed in the present settings, the study revealed a drastic reduction in survival probability, i.e., from 90% to 79% in the last year of follow-up period. However, the cumulative survival probability over the five-year observation period was 79%. It was discovered that patients who received the TLE regimen for a longest period were found to be 2.83 times more vulnerable to death compared with others. However, no significant side effects were reported among those who received the TLE regimen. As there is no supportive literature on this matter, we recommend that in-depth or experimental studies to be conducted in the future to explore the issue. It is important to prioritize the exploration of the TLE ART regimen, despite its potential link to higher mortality rates among patients who received it for a longer period of time. While ART has been proven to increase survival probability and quality of life of HIV patients in different studies, it is crucial to continually adapt healthcare practices and provide effective regimens to ensure the best possible outcomes for those living with the virus in rural areas.

Further research and investigations can help shed light on the issue and inform healthcare providers on the most effective treatment options. It is important for healthcare providers to continually adapt their practices and provide effective ART regimens for patients living with HIV in rural areas to ensure their survival probability.

Disclosures

1. Institutional review board statement: The study was approved by the Ethics Committee of the Bankura Sammilani Medical College, Bankura (approval letter number: BSMC/IEC: 847, dated 05/04/2022).
2. Assistance with the article: The authors are thankful and would like to express their gratitude to all medical and paramedical staff of the ART center, who helped to collect the secondary data source for the study within hectic time schedule. We are also immensely grateful to the ICMR (Indian Council of Medical Research) – Short Term Studentship (STS) 2022 Program, for providing such opportunity and motivation in research work. Last but not least, we are thankful to all PLWHA whose data were used in the study. Many of them are not with us

anymore in person, but remain alive through their contribution to this study.

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4. Conflicts of interest: None.

References

1. UNAIDS. Global HIV & AIDS statistics – Fact sheet. Available from: <https://www.unaids.org/en/resources/fact-sheet> (Accessed: 30.07.2023).
2. Johnson SC. Antiretroviral therapy for HIV infection: when to initiate therapy, which regimen to use, and how to monitor patients on therapy. *Top Antivir Med* 2016; 23: 161-167.
3. Mbirintengerenji ND. Is HIV/AIDS epidemic outcome of poverty in sub-saharan Africa? *Croat Med J* 2007; 48: 605-617.
4. National AIDS Control Organisation. HIV Facts & Figures. Available from: <https://naco.gov.in/hiv-facts-figures> (Accessed: 30.07.2023).
5. Moosavi S, Pokorny KL, Poorolajal J, Mahjub H. Fuzzy survival analysis of AIDS patients under ten years old in Hamadan-Iran. *J Intell Fuzzy Syst* 2015; 28: 1385-1392.
6. Tadesse K, Haile F, Hiruy N. Predictors of mortality among patients enrolled on antiretroviral therapy in Aksum hospital, northern Ethiopia: a retrospective cohort study. *PLoS One* 2014; 9: e87392. DOI: 10.1371/journal.pone.0087392.
7. Celesia BM, Castronuovo D, Pinzone MR, Bellissimo F, Mughini MT, Lupo G, et al. Late presentation of HIV infection: predictors of delayed diagnosis and survival in Eastern Sicily. *Eur Rev Med Pharmacol Sci* 2013; 17: 2218-2224.
8. Biadgilign S, Reda AA, Digaffe T. Predictors of mortality among HIV infected patients taking antiretroviral treatment in Ethiopia: a retrospective cohort study. *AIDS Res Ther* 2012; 9: 15. DOI: 10.1186/1742-6405-9-15.
9. Siraj M, Gedamu S, Tegegne B. Predictors of survival time among HIV-infected adults after initiating anti-Retroviral therapy in kombolcha town: a 5-year retrospective cohort study. *HIV AIDS (Auckl)* 2022; 14: 181-194.
10. Chanie ES, Gelaye GA, Tadesse TY, Feleke DG, Admas WT, Molla Alemu E, et al. Estimation of lifetime survival and predictors of mortality among TB with HIV co-infected children after test and treat strategies launched in Northwest, Ethiopia, 2021; a multicentre historical follow-up study. *PLoS One* 2021; 16: e0258964. DOI: 10.1371/journal.pone.0258964.
11. Pahari S, Roy S, Mandal A, Kuila S, Panda S. Adherence to anti-retroviral therapy & factors associated with it: a community based cross-sectional study from West Bengal, India. *Indian J Med Res* 2015; 142: 301-310.
12. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med* 2000; 133: 21-30.
13. Poorolajal J, Hooshmand E, Mahjub H, Esmailnasab N, Jenabi E. Survival rate of AIDS disease and mortality in HIV-infected patients: a meta-analysis. *Public Health* 2016; 139: 3-12.
14. Varni SE, Miller CT, McCuin T, Solomon S. Disengagement and engagement coping with HIV/AIDS stigma and psychological well-being of people with HIV/AIDS. *J Soc Clin Psychol* 2012; 31: 123-150.
15. Kaneez S. Depression and coping mechanism among HIV/AIDS patients under anti-retroviral therapy. *Ind J Soc Psychiatr* 2016; 32: 149. DOI: 10.4103/0971-9962.181098.
16. Jain D, Kumar J, Katyal VK, Jain P, Malik D. Evaluation of depression, anxiety and insomnia in people living with HIV/AIDS in India. *HIV AIDS Rev* 2023; 22: 138-149.
17. Rajasekar V, Thirunaaukarasu D, Surendar R. Socio-demographic profile and adherence to anti-retroviral treatment among HIV/AIDS patients attending the ART centre in Tamil Nadu. *J Med Sci Health* 2023; 9:163-168.

18. Kumar P, Sahu D, Chandra N, Kumar A, Rajan S. Aging of HIV epidemic in India: insights from HIV estimation modeling under the National AIDS Control Programme. *Indian J Public Health* 2020; 64: 76-78.
19. Mehta KG, Baxi R, Patel S, Parmar M. Drug adherence rate and loss to follow-up among people living with HIV/AIDS attending an ART Centre in a Tertiary Government Hospital in Western India. *J Family Med Prim Care* 2016; 5: 266-269.
20. Akbari M, Fararouei M, Haghdoost AA, Gouya MM, Kazerooni PA. Survival and associated factors among people living with HIV/AIDS: a 30-year national survey in Iran. *J Res Med Sci* 2019; 24: 5. DOI: 10.4103/jrms.JRMS_630_18.
21. Mohammadi Y, Mirzaei M, Farhadian M, Poorolajal J, Kazerooni P, Tayeri K. Survival rate and the determinants of progression from HIV to AIDS and from AIDS to the death in Iran: 1987 to 2016. *Asian Pac J Trop Med* 2019; 12: 72. DOI: 10.4103/1995-7645.250840.
22. Manosuthi W, Charoenpong L, Santiwarangkana C. A retrospective study of survival and risk factors for mortality among people living with HIV who received antiretroviral treatment in a resource-limited setting. *AIDS Res Ther* 2021; 18: 71. DOI: 10.1186/s12981-021-00397-1.
23. Moradi A, Hashemi Nazari SS, Zandvakili F, Ameri P, Nikfarjam A, Darvishi S, et al. Survival rate of patients with HIV/AIDS and related factors in Tehran, Iran. *Shiraz E Med J* 2020; 21. DOI: 10.5812/semj.98500.
24. Badii VS, Buabeng KO, Agyarko Poku T, Forkuo AD, Boamah BB, Arhin SM, et al. Tenofovir-based highly active antiretroviral therapy is associated with superior CD4 T cells repopulation compared to zidovudine-based HAART in HIV 1 infected adults. *Int J Chronic Dis* 2018; 2018: 3702740. DOI: 10.1155/2018/3702740.
25. Singla R, Sharma N. A comparative evaluation of the effects of ZLN and TLE anti-retroviral regimens in HIV positive patients: a retrospective record-based study. *Indian J Physiol Pharmacol* 2021; 64: 298-302.
26. Bansal R, Ashahiya ID. Comparison between two regimens of art in human immunodeficiency virus patients at Tertiary Care Art Centre Jabalpur: a prospective observational study. *Int J Sci Study* 2018; 6: 62-66.
27. 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: 357-366.
28. Moses K, Adefisayo OA, Maryam B, Adeoye A, Oluwatosin A, Abiye K, et al. Virologic response among key populations living with HIV following a switch to dolutegravir-based regimen in southern Nigeria. *Int J Virol AIDS* 2020; 7. DOI: 10.23937/2469-567x/1510069.
29. Paul NI, Ugwu RO. Dolutegravir (DTG) based fixed dose combination (FDC) of tenofovir/lamivudine/dolutegravir (TLD) and viral load suppression in children in Port Harcourt, Nigeria. *J Sci Res Rep* 2020. DOI: 10.9734/jsrr/2020/v26i230224.
30. Fettiplace A, Stainsby C, Winston A, Givens N, Puccini S, Vannapagari V, et al. Psychiatric symptoms in patients receiving dolutegravir. *J Acquir Immune Defic Syndr* 2017; 74: 423-431.