

# Increased Virological Failure and Determinants Among HIV Patients on Highly Active Retroviral Therapy in Adigrat General Hospital, Northern Ethiopia, 2019: Hospital-Based Cross-Sectional Study

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**Background:** In Ethiopia, despite the integrated implementation of antiretroviral therapy since 2005, the human immunodeficiency virus remains a public health concern. Managing and detecting antiretroviral treatment response is important to monitor the effectiveness of the therapy for individuals who experience failed virological response. An increased viral load indicating drug resistance or rapid progression of viral replication needs early detection. Hence, we aimed to assess the prevalence and determinants of virological response among human immunodeficiency virus-infected patients on highly active antiretroviral therapy.

**Methods:** A hospital-based cross-sectional study was conducted in Adigrat General Hospital from September to December, 2019, on a total of 422 participants. An interviewer-based questionnaire was used for data collection. About 4 mL of venous blood was collected for viral load determination. Patient records were reviewed for the previous results of CD4+ T cell counts. STATA 14 software was used to analyze the data. Descriptive data were presented using tables and figures. Bivariate and multivariate analyses were performed. A p-value < 0.05 was considered a statistically significant association.

**Results:** The mean age of study participants was 39 years (SD ±12.2 years), of which 66.7% of them were females. The overall prevalence of virological failure was 12.47% (49/393). Moreover, the prevalence of virological failure was observed to be higher among tuberculosis co-infected individuals (26%) compared with the mono-infected HIV patients (6.3%). The odds of virological failure were higher among obese and undernourished individuals, tuberculosis co-infected, and individuals with the failure of immune reconstitution.

**Conclusion:** There was a high rate of virological failure among the study participants. Tuberculosis infection increased the rate of failure. There should be consistent assessment of viral load testing to determine the status of virological response for appropriate drug switching to clients. HIV patients with virological failure are recommended for switching of the antiretroviral therapy.

**Keywords:** Ethiopia, prevalence, HAART, HIV, HIV/TB co-infection, virological failure

## Introduction

Human immune-deficiency virus (HIV) continues to be one of the top public health priorities in Ethiopia.<sup>1</sup> By the end of 2013, there were a total of 593,400 adults living with HIV of which only 298,512 were on highly active antiretroviral therapy

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(HAART). Moreover, an estimated 45,200 people died due to HIV-related conditions in 2013.<sup>2</sup> HAART is a life-saving treatment for patients with HIV which is an important component of the overall treatment plan among HIV patients.<sup>3</sup> Since the introduction of HAART, the impact of HIV infection has significantly decreased<sup>4</sup> due to viral suppression, restoring and preserving immune function, improving quality of life, and reducing HIV related morbidity and mortality along the course of treatment.<sup>5-7</sup>

Globally, many reports revealed that HIV infected individuals are experiencing virological, clinical, and immunological treatment failures.<sup>7</sup> Virological failure, which is more suggestive of treatment failure of HAART, is a common problem that an HIV infected individual faces after starting treatment. Current World Health Organization (WHO) guidelines recommend that virological failure should not exceed 10% RNA copies per mL of plasma from the initiation of HAART.<sup>8</sup> Patients who have experienced virological failure were found to have an increased risk of clinical progression to acquired immune deficiency syndrome (AIDS) and mortality compared with patients with virological success.<sup>9</sup> Previous studies reported various factors like baseline CD4+ T cell counts,<sup>5,9-11</sup> being younger,<sup>12-14</sup> longer duration on HAART,<sup>10,13,15</sup> poor adherence to treatment<sup>12,13,16,17</sup> and current lower CD4+ T cell counts<sup>15,18</sup> as associated with virological failure.

The introduction of combination therapy<sup>19,20</sup> has modified the natural history of HIV infection from an end of life event to a manageable chronic condition<sup>21</sup> thereby changing the landscape of HIV related mortality. Despite the benefits of HAART, it is not without challenges. There are many adverse drug reactions (ADRs) associated with HAART treatment resulting in negative health outcomes<sup>22,23</sup> and increased mortality.<sup>24</sup> Treatment discontinuation and medication non-adherence associated with ADRs are significant risk factors to catalyze virological failure.<sup>25,26</sup> HAART failure to first-line regimens resulting from ADRs creates the need for very expensive and difficult-to-implement second-line regimens. Second-line HAART regimens are often unaffordable and largely donor dependent in resource-limited settings.<sup>27</sup>

The United Nations program on HIV/AIDS (UNAIDS) is aimed at the “90-90-90 target” to maintain viral suppression in 90% of persons on HAART by 2020.<sup>28</sup> An important strategy to achieve this target, apart from the promotion of treatment adherence, is the use of a safer HAART regimen to promote maximal viral suppression and immune reconstitution.<sup>29,30</sup> Identifying and managing determinants of virological failure

have an important role in achieving high treatment success, improving the quality of life, and increasing survival rate from treatment failure. However, there is limited evidence on the epidemiology of virological failure among HIV infected individuals on HAART in the study area. Thus, this study aimed to identify the prevalence and determinants of virological failure among HIV-infected individuals on HAART in Adigrat General Hospital, Northern Ethiopia.

## Methods

### Study Design, Area and Period

A hospital-based cross-sectional study was employed to assess the prevalence of virological failure and determinants among HIV infected individuals on highly active retroviral therapy in Adigrat General Hospital, Eastern Tigray, Ethiopia from September to December 2019.

Adigrat General Hospital is one of the governmental Hospitals located in Adigrat Town and was established to serve people from 6 weredas (districts). The Hospital is currently providing teaching and referral services for a population of more than 1,000,000 with an average annual client flow of 131,125 people.<sup>31</sup> The Hospital has about 120 beds with a total of 209 health care providers and 132 administrative staff. There are 10 health care providers in the HAART clinic of the Hospital with a total of 1582 HIV patients currently on HAART. There is also an integrated service of ART clinic, laboratory services and pharmacy department. CD4+ T cell and viral load determinations are being used to monitor the effectiveness of HAART therapy with additional laboratory tests like complete blood cells and chemistry tests.

### Source Population

- All HIV infected individuals on HAART who were attending Adigrat General Hospital.

### Study Population

- All HIV infected individuals on HAART who attended appointments at the HAART clinic in the hospital during the study period.

### Sampling Technique and Sample Size

- A convenience sampling technique was used to enroll the study participants among HIV infected individuals on HAART.
- The sample size was calculated using a single population proportion and determined using the following

assumptions 95% CI, 5% margin of error and considering 50% prevalence rate.

Then total sample size  $(n) = (Z_{\alpha/2})^2 (p) (1-p)/d^2 = (1.96)^2 (0.5) (0.5)/0.05 = 384$

While  $(Z_{\alpha/2} = 1.96)$ ,  $p$  is estimated prevalence (50%) and  $d$  is margin of error (5%) which Finally, after adding 10% non-response rate 422 study participants were enrolled.

## Eligibility Criteria

### Inclusion Criteria

- HIV infected individuals with at least 6 months of follow-up on HAART
- HIV infected individuals who have provided written informed consent for individuals greater than 18 years of age or those individuals less than 18 years who have informed consent from a parent/guardian.

### Exclusion Criteria

- HIV patients who were critically ill and unconscious
- HIV infected individuals with incomplete charts

### Dependent Variable

- Virological response

### Independent Variables

- Age, sex, intake of modern contraceptives, residence, adherence to treatment, co-infection with tuberculosis, marital status, educational status, body mass index, functional status, baseline CD4+ T cell count, WHO stage, presence of opportunistic infections

## Data Collection, Preparation, and Analysis

### Data Collection

An interviewer-based semi-structured questionnaire was used to collect socio-demographic data (age, sex, modern contraceptive intake, BMI, and residence). Clinical data (duration of HAART, current adherence to HAART, TB co-infection, eligibility criteria, cotrimoxazole intake, functional status, WHO stage, TB status, and presence of opportunistic infections) and previous results of CD4+ T cell counts for each patient were collected from patients' medical records and through the questionnaire.

### Sample Collection, Transportation, and Viral Load Determination

About 4 mL of venous blood was collected from each patient by trained laboratory professionals using EDTA

vacutainer tube. Plasma was separated by centrifugation at 1500 rpm for 10 minutes and transferred into a sterile screw-capped polypropylene (Cryo) tube. The plasma specimens were then frozen at  $-20^{\circ}\text{C}$  and transported to Tigrai Research and Health Institute (THRI) adhering to the cold chain processes within 3 days of collection for viral load determination. To ensure the safety of the plasma specimens we applied triple packaging and labelled with UN3373. In the THRI, HIV-1 RNA was extracted from each patient's plasma using the Abbott m2000sp automated sample preparation system (Abbott Molecular™, USA). Further RNA quantitative determination was performed using Abbott m2000rt quantitative Real-Time HIV-1 assay (Abbott Molecular™, USA) with a detection level of 40 to 10 million RNA copies/mL.

## Data Analysis

We used STATA Version 14 software for data entry and analysis. Descriptive statistics were performed. Data were summarized and organized using figures and frequency tables. Bi-variate and multi-variate regression analysis were employed to measure the association between dependent and independent variables using backward model analysis. Variables with  $p < 0.2$  in the bivariate logistic regression were imported to multi-variate regression analysis to identify the factors that have statistical significance in relation to the dependent variable. In the multivariate analysis, multicollinearity was considered by performing variance inflation factor (VIF) to indicate the correlation of independent variables to each other. Additionally, Hosmer-Lemeshow goodness of fit statistic was considered for the logistic regression. A  $p$ -value of  $< 0.05$  was considered statistically significant.

## Quality Control

Quality of laboratory data was maintained by strictly following standard operational procedures (SOPs) during sample collection, handling, and transportation. Quality control reagents were included in each test to evaluate the run validity of the viral load determination. Furthermore, viral load reagents were checked for expiry date. Questionnaires were checked for completeness and consistency on a daily bases during data collection by the principal investigator. Patient records were managed for confidentiality.

## Operational Definition

### Treatment Adherence

Taking HAART medications properly on a consistent basis over time and not missing doses of the prescribed therapeutic agents.<sup>8</sup>

- Good adherence: When the average treatment adherence of HIV patients is greater than or equal to 95%.
- Average Adherence: The average treatment adherence by the patients is from 85% to 94%.
- Weak Adherence: The average treatment adherence by the patients is less than 85%.

### Immune Reconstitution

The ability of the body to respond to HAART and recovery of CD4+ T cell counts.

- Failure in Immune Reconstitution: CD4+ T cell counts to baseline or below/CD4+ T cell counts below 100 cells/mm<sup>3</sup> for consecutive tests during the course of HAART.<sup>8</sup>
- Success in immune reconstitution: CD4+ T cell counts greater than the baseline count after initiation of HAART.<sup>8</sup>

### Virological Failure

When the viral load of the HIV infected individual is greater than 1000 copies/mL of plasma which is determined based on two consecutive viral load measurements with adherence support.<sup>32</sup>

## Results

### Socio-Demographic Characteristics of Patients

A total of 422 HIV infected individuals on HAART were enrolled in our study, yielding an overall response rate of 93.1% (393/422). Out of the total study participants, 262 (66.7%) were females. The mean age of the study participants was 39 years ranging from 5 to 78 years. The participant had been followed in the clinic from 6 to 180 months with a median of 121 months and IQR of 66 to 132. Nearly two-thirds (249/393) of the study participants were urban dwellers.

### Baseline Clinical Characteristics of Patients

The majority of study participants, 80% (314), were linked to HAART due to clinical staging. One hundred twenty-three (31.3%) of the total study participants were observed to be

co-infected with TB. Most of the study participants, 89.1% (350/393), were in WHO clinical stage I. The overall virological failure of HIV patients in our study was 12.5% (49/393) (Table 1). One-hundred ninety-four (49.4%) of the study participants had opportunistic infections, such as: intestinal parasitic infections [24.23%, 47/194], fungal infections [9.3%, 18/194], varicella-zoster [6.19%, 12/194], pneumonia [5.67%, 11/194], upper respiratory tract infection [4.12%, 8/194] and urinary tract infections [3.61%, 7/194].

### Comparison of Virological Failure Among Tuberculosis Co-Infected and Mono-Infected Clients

From this study, the prevalence of virological failure among HIV/TB co-infected patients was 26% (32/123) compared to 6.3% (17/270) amongst HIV mono-infected patients (Figure 1).

### Prevalence and Determinants of Virological Failure of HAART Among HIV Patients

The overall prevalence of virological failure was 12.47% (49/393). Increased virological failure was observed among clients with overweight body mass index [AOR = 1.19, 95% CI: [0.290–1.717], p = 0.001], being malnourished [AOR = 2.1, 95% CI: [1.322–8.271], p = 0.001], individuals with tuberculosis infection [AOR = 6.1, 95% CI: 3.000,12.223, p < 0.001] and immunological treatment failure [AOR = 19.4, 95% CI: [0.019, 20.129], P = 0.049] (Table 1).

## Discussion

In this current study, the overall virological failure of HAART treatment was 12.47% (49/393). This finding aligned with a number of studies previously conducted in Ethiopia such as: in Tigray, 11.5%,<sup>33</sup> Gondar, 11.8% and 14.7%,<sup>18,34</sup> Bahir Dar, 10.7%<sup>35</sup> and Addis Ababa 15%.<sup>36</sup> Studies outside of Ethiopia showing similar rate of virological failure were found in Zambia 12.3%,<sup>37</sup> Tanzania, 12.3%,<sup>38</sup> Malawi, 9.2%,<sup>39</sup> Nigeria, 13.7%,<sup>40</sup> South Africa, 13.7%,<sup>41</sup> Uganda, 9.9%, 11.3% and 14.15%,<sup>42–44</sup> New Guinea, 13.7%,<sup>45</sup> China, 13.4%,<sup>46</sup> Thailand, 9.6%,<sup>47</sup> Nepal, 9.9%,<sup>48</sup> and Cambodia, 12.9%.<sup>49</sup> The result of the current study was higher for virological failure than previously conducted research in Ethiopia (i.e., Jimma, 5.3%<sup>50</sup> and Gondar, 4.1%<sup>51</sup>) and Burkina Faso at 7.5%.<sup>52</sup> However; our finding was lower than the other studies done in Cameroon, 23.2%<sup>53</sup> and Kenya, 24%,<sup>54</sup> Liberia,

**Table 1** Demographic, Baseline, Clinical Characteristics, Bivariate and Multivariate Analysis of Determinant Factors with a Virological Response of HAART Among HIV Patients in Adigrat General Hospital, Eastern Tigray, Ethiopia, 2019: A Cross-Sectional Study (n = 393)

Variables		Virological Response		P value	COR	CI	P value	AOR	CI
		Success, N (%)	Failure, N (%)						
Sex	Male	111 [84.7]	20 [15.3]	0.237	1	[0.784–2.672]			
	Female	233 [88.9]	29 [11.1]		1.5				
Age category	<15 years	16 [72.7]	06 [7.3]	0.000	5.8	[3.019–13.345]	0.750	0.6	[0.030–12.644]
	15–30 years	40 [83.3]	08 [16.7]	0.001	5.6	[2.641–11.873]	0.767	0.7	[0.101–5.409]
	31–45 years	184 [89.8]	21 [10.2]	0.011	2.3	[1.209–4.467]	0.724	0.8	[0.278–2.436]
	46–60 years	92 [86.8]	14 [13.2]	0.179	1.6	[0.810–3.076]	0.329	1.5	[0.674–3.246]
	>60 years	12 [100]			1			1	
Marital status	Single	85 [85.9]	14 [14.1]	0.502	1.4	[0.972–2.341]			
	Married	169 [89.4]	20 [10.6]	0.873	1	[0.493–3.562]			
	Widowed	41 [85.4]	7 [14.6]	0.461	1.5	[0.703–2.992]			
	Divorced	49 [86.0]	8 [14.0]	0.694	1.4				
Educational status	Illiterate	136 [84.0]	26 [16]	0.324	2.4	[1.001–5.231]			
	Read and write	48 [85.7]	8 [14.3]	0.543	2.1	[0.928–4.908]			
	Primary school	96 [90.6]	10 [9.4]	0.608	1.3	[0.104–2.093]			
	Secondary/above	64 [92.8]	5 [7.2]	0.671	1				
Residence	Urban	215 [86.3]	34 [13.7]	0.351	1.4	[0.713–2.594]			
	Rural	129 [89.6]	15 [10.4]		1				
BMI	Normal	199 [88.8]	25 [11.2]	0.009	1	[0.281–0.667]	0.001	1	[0.290–1.717]
	Overweight	35 [94.6]	02 [5.4]	0.001	0.6	[1.097–5.453]	0.001	1.19	[1.332–8.271]
	Undernourished	110 [83.3]	22 [16.7]		2			2.1	
Cotrimoxazole intake	No	68 [85]	12 [15]	0.444	0.8	[0.376–1.535]			
	Yes	276 [88.2]	37 [11.8]		1				
Eligibility criteria	Clinical staging	273 [86.9]	41 [13.1]	0.034	1	[0.879–6.301]	0.066	1	[0.077–1.084]
	Test and treat	19 [79.2]	05 [20.8]	0.101	3	[0]	0.062	0.3	[0.038–1.085]
	Transferred in	52 [94.5]	03 [5.5]		1.7	[0.906–3.018]		0.2	
Functional status	Working	319 [87.6]	45 [12.4]	0.187	1	[0.614–12.115]	0.492	1	[0.403–6.621]
	Ambulatory	22 [84.6]	4 [15.4]	0.273	2.7	[0.671–3.109]	0.999	1.6	[0.989–5.768]
	Bedridden	03 [100]			1.6			3.6	
Base line CD4 < 250	Yes	214 [88.4]	28 [11.6]	0.496	0.8	[0.442–1.485]			
	No	130 [86.1]	21 [13.9]		1				
WHO stage	Stage I	307 [87.7]	43 [12.3]	0.072	1	[0.910–8.771]	0.772	1	[0.316–2.350]
	Stage II	19 [90.5]	02 [9.5]	0.470	2.8	[0.496–4.565]	0.949	0.9	[0.193–5.778]
	Stage III	14 [82.4]	03 [17.6]	0.238	1.5	[0.891–5.723]	0.426	1.1	[0.193–49.317]
	Stage IV	04 [80]	01 [20]		2.1			3.1	
Modern contraceptive	No	200 [88.1]	27 [11.9]	0.687	1	[0.620–2.067]			
	Yes	144 [86.7]	22 [13.3]		1.2				
Adherence to treatment	Good	256 [89.8]	29 [10.4]	0.010	1	[1.193–3.777]	0.823	1	[0.325–4.116]
	Average	25 [83.3]	05 [16.7]	0.005	2.1	[2.674–10.439]	0.137	1.2	[0.832–3.818]
	Weak	63 [80.8]	15 [19.2]		3.9			1.8	

(Continued)



Table I (Continued).

Variables		Virological Response		P value	COR	CI	P value	AOR	CI
		Success, N (%)	Failure, N (%)						
Opportunistic infections	Yes	165 [85.1]	29 [14.9]	0.144	1.6	[0.857–2.888]	0.103	1.8	[0.892–3.444]
	No	179 [90]	20 [10]						
Status TB	Positive	91 [74]	32 [26]	0.000	5.2	[2.773–9.877]	< 0.001	6.1	[3.000–12.223]
	Negative	253 [93.7]	17 [6.3]						
Immune-reconstitution status	Success	286 [96.6]	10 [3.4]	0.000	1	[0.025–19.110]	0.049	1	[0.019–20.129]
	Failure	58 [59.8]	39 [40.2]						

Abbreviations: AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; COR, crude odds ratio; TB, tuberculosis; WHO, World Health Organization.

47%,<sup>55</sup> Zimbabwe, 30.6%,<sup>56</sup> Tanzania 57.1%,<sup>57</sup> 32%,<sup>58</sup> Cameroon, 20.6%,<sup>59</sup> Ghana, 16.7%,<sup>60</sup> Togo, 51.6%,<sup>61</sup> Colombia, 20.9%,<sup>62</sup> India, 69.6%<sup>63</sup> and Peru, 24%.<sup>64</sup> This variance might be attributed due to differences in cutoff values of viral RNA copies per mL of plasma to be considered as virological failure, the difference among study participants, duration of follow-up, study design, and variations on the treatment adherence of HAART. Moreover, protease inhibitors were used as the first-line HAART regimen<sup>52</sup> and nutritional support given for the study participants<sup>50</sup> which were different from our setting, difference in a geographical area, study design, and the virological failure cutoff points, in our study, was a plasma viral load  $\geq 400$  copies/mL,<sup>54,57,65</sup> inclusion criteria used, study participants were clinically/immunologically

failed,<sup>55,66</sup> perinatally infected,<sup>61</sup> lower mean age<sup>59</sup> and shorter mean time on HAART.<sup>60</sup>

Two hundred eighty-five (72.5%) of our study participants had good adherence to treatment. Similar adherence trends were seen in previous studies across Ethiopia including Southern Ethiopia, 81.8%,<sup>36</sup> Northwestern Ethiopia, 82.7%<sup>67</sup> and Addis Ababa, Ethiopia, 78.5%.<sup>68</sup> However, our study reported lower treatment adherence than select studies conducted in Addis Ababa, Ethiopia, 97.7%<sup>69</sup> and Southwestern Ethiopia, 100%.<sup>50</sup> These variations in patient adherence might be due to differences in psychosocial support of relatives or the society, stigma, and lack of commitment to take medications so that HIV patients might drop from the HAART treatment, after not feeling well (perceived it from the medication), fear of treatment side effects, and being busy (forgetting the HAART medication).<sup>8,34</sup>

Malnourished and overweight HIV infected individuals were 2.1 ( $p = 0.001$ ) and 1.19 ( $p = 0.001$ ) times high likely to experience virological failure than individuals with normal body mass index. This finding aligns with previous studies from Northwestern Ethiopia<sup>34</sup> and Northwestern Uganda.<sup>70</sup> It is evident that abnormal BMI is correlated significantly with the decrease in CD4+ T cell count and the increase in viral load by progressing into the advanced stage of the disease, and by exposing the patients not taking ART medication (poor adherence).<sup>71,72</sup>

This study revealed that virological failure was 6.1 times more likely to occur among TB co-infected individuals than the TB non-infect cohort ( $p < 0.001$ ). This was similar to reports from Uganda,<sup>73</sup> South Africa.<sup>74,75</sup> It is possible for virological failure to lead to incident TB. The risk of virological non-suppression may also be increased by concurrent ART and TB treatment due to impaired treatment adherence

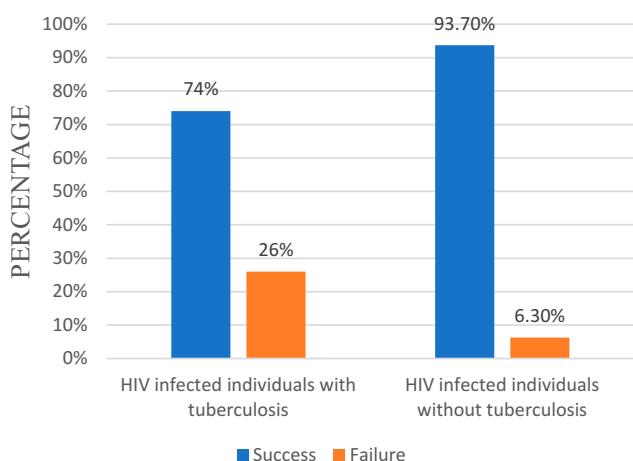


Figure 1 Prevalence of virological failure among HIV patients co-infected with tuberculosis and HIV mono-infected individuals on HAART in Adigrat General Hospital, Eastern Tigray, Ethiopia, 2019: a cross-sectional study (n = 393).

Abbreviations: HIV, human immunodeficiency virus; HAART, highly active antiretroviral therapy.

and pharmacokinetics drug interactions. Patients on ART with active TB should be prioritized for viral load monitoring and adherence support. Strengthening interventions that prevent incident TB during ART, such as isoniazid prevent therapy and infection control at health facilities, is crucial. A possible explanation for this might be increased viral copies which may compromise immunity and negatively affect response to treatment by contributing to the double burden side effects of tuberculosis and HIV.<sup>76</sup>

Individuals with failure of immune reconstitution were observed to be at increased risk of experiencing immunological failure of HAART ( $p = 0.049$ ). This finding was identified in previous studies from India,<sup>77</sup> Northwestern Ethiopia<sup>78</sup> and Brazil.<sup>79</sup> The failure of immune reconstitution leads to the rapid progression of viral antigen replication.<sup>80</sup> Failure in immune reconstitution should also be a surrogate marker for virological failure. Hence, detection and monitoring immunological response of CD4 + T cells for immune reconstitution should be intensified largely to prevent resistance to antiretroviral therapy.<sup>80,81</sup>

## Strength and Limitation of the Study

The strength of the study is that both CD4+ T cell counts and viral load determination were assessed for each HIV infected individual on HAART to determine the response to immune reconstitution and virological failure. Despite this approach, the viral load to determine the virological response was performed only once. We should have performed two consecutive measurements to strengthen the findings.

## Conclusion

The overall prevalence of virological failure among HIV patients on HAART was high. Factors such as being obese, malnourished, tuberculosis co-infected and failure in immune reconstitution were also associated with virological failure. The virological response should be regularly performed as per the WHO guideline in order to ensure early detection of drug resistance and to respond with the possibility of regimen switching. It is apparent that virological and immunological response in cases of suspected along with clinical failures should be performed simultaneously.

## Abbreviations

ADRs, adverse drug reactions; AIDS, acquired immune deficiency syndrome; HAART, highly active antiretroviral

therapy; HIV, human immunodeficiency virus; UNAIDS, United Nations on HIV/AIDS.

## Data Sharing Statement

All datasets generated and/or analyzed during the current study are summarized in the manuscript.

## Ethics Approval and Consent to Participate

Ethical clearance was obtained from the research and community service committee of Adigrat University with a reference number of Adigrat University/College of Medicine and Health Science/085/19. Official letters were obtained from Tigray Regional Health Bureau, Tigray Research and Health Institute, the Chief Executive Officer of Adigrat Hospital, Department of Patient Records, and Laboratory Head in Adigrat Hospital before the data collection. Written informed consent was sought from each study participant with parents or guardians consenting for participants aged less than 18 years. Data of every HIV patient on HAART were kept confidential. This study was conducted in accordance with the declaration of Helsinki.

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## Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, drafting the manuscript, revising the manuscript critically, read and approve the final draft of the manuscript for submission, gave final approval of the manuscript version to be published and agreed to be accountable for every step of the work.

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## Disclosure

The authors declared they have no competing interests.

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