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Factors associated with immunological and virological discordant responses to highly active antiretroviral therapy among adult HIV positive individuals in Ethiopia

A cross-sectional study

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Abstract

In clinical practice, not all human immune deficiency virus (HIV) positive individuals who received highly active antiretroviral therapy (HAART) achieve the desired concordant response characterized by a sustained viral suppression or immune recovery. The expected success of HAART doesn't occur in all treated patients and a discordant response between CD4 count and the viral load (VL) has been a major concern in the treatment of HIV patients. Thus, this study is designed to describe the factors associated with immunological and virological discordant responses to HAART among adult HIV positive individuals.

A hospital-based cross-sectional study with secondary data review was conducted on 423 HIV positive individuals on HAART from February 1 to April 30, 2017. Socio-demographic characteristics, clinical data and about 10 mL of blood specimen for HIV VL, and CD4 count measurement were collected. The data was entered into SPSS version 20 and descriptive, bivariate, and multivariate logistic regression analysis was employed.

The mean age of the patients at study time was 39 (±9.8). The average follow-up duration of patients on antiretroviral therapy (ART) was 7 (±3) years. The prevalence of immunological discordance and virological discordance to HAART were 13.2% and 47%, respectively. With multivariate logistic regression analysis duration of follow-up on ART ≤ 6 years (adjusted odds ratio [AOR] = 3.29 (1.80–6.03), $P \leq .001$) and VL ≥20 copies/mm^3 (AOR = 3.08 [1.70–5.61], $P \leq .001$) were significant factors for immunological discordance conversely the patients who switched drug as a result of TB (AOR = 3.33 [1.10–10.08], $P = .03$) was significant factors for virological discordance.

The prevalence of immunological discordance and virological discordance to HAART among HIV patients is high. Patients with the duration of follow-up on ART ≤ 6 years, VL ≥ 20 copies/mm^3 and patients who switched drugs as a result of TB were significant factors for discordance. Hence, intensive adherence support and counseling should be provided to achieve the UNAIDS 90 target. HIV positive individuals co-infected with TB, who have had VL ≥ 20 copies/mm^3 and who are ≤6 years duration of follow-up on ART need to be carefully monitored. In addition, national based study of discordant groups is recommended.

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Ethical clearance was obtained from the Research and Ethical Review Committee of the School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar. The permission letter was taken from the clinical director of the University of Gondar Specialized Referral Hospital. Written informed consent was obtained from each study participant after reading and clearly explaining the reason, procedure, period, possible risks, the privacy of personal information and benefits of the research in Amharic translated full participant information sheet. Patients who were not willing to participate in the study were not forced to take part in the study. The privacy of personal information was protected and kept confidential by excluding their name during data collection. The laboratory results of the study participants were communicated to their physicians for appropriate medical management.

Consent for publication is not applicable

The data used to support the findings of this study are available from the corresponding author upon request.

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Abbreviations: AIDS = acquired immune deficiency syndromes, AOR = adjusted odds ratio, ART = antiretroviral therapy, HAART = highly active antiretroviral therapy, HIV = human immune deficiency virus, SOP = standard operational procedure, UOGRH = University of Gondar Referral Hospital, VL = viral load, WHO = World Health Organization.

Keywords: discordant, highly active antiretroviral therapy, human immune deficiency virus/acquired immune deficiency syndromes, immunological discordant, virological discordant

1. Introduction

The introductions of highly active antiretroviral therapy (HAART) in the late 1990s significantly reduce the morbidity and mortality associated with human immune deficiency virus (HIV) infection.[1] This reduction is due to the ability of HAART to suppress HIV viral load (VL) and allowing the recovery of an immune response (CD4+ count). An effective HAART is immune reconstitution (increased CD4+ count) and virologic suppression (an undetectable VL).[2] However, in clinical practice, not all patients who received HAART achieve the desired concordant response characterized by a sustained ether viral suppression or immune recovery with HAART. Since the expected success of HAART doesn't occur in all HIV treated patients, immunological and virological nonresponse to HAART, and a discordant response between CD4+ count and the VL has been a major concern. As many as 20% to 40% and 10% to 23% of patients on antiretroviral therapy (ART) do not show a significant increase in CD4+ count and undetectable level in the VL, respectively.[3,4] These phenomenon's are referred to as immunological discordant response (not show a significant increase in CD4+ count) and virological discordant responses (above the undetectable level in the VL). Those are associated with an increased risk of developing an acquired immunodeficiency syndrome (AIDS) event or death.[3–7] The discordant immune response may arise either as a result of failed immune reconstitution or the excessive destruction of CD4 cells or viral resistance.[8]

The problem should be under consideration in sub-Saharan Africa where the majority of people living with HIV located. Potentially, the problems may become a challenge to achieve the 90-90-90 ambitious plan. Relative frequency of either immunological or virological discordance response following HAART initiation and associated factors are still limited in Ethiopia, in low and middle-income countries too. So the lack of data about either immunological or virological discordance response may contribute to inadequate clinical management, as current HIV treatment guidelines do not provide specific applicable guidance. In this cross-sectional study, we describe factors associated with discordant immunological and virological response.

2. Materials and methods

2.1. Aim

The aim of this study was to assess the prevalence of and factors associated with immunological discordance response to HAART and to assess the prevalence of and factors associated with virological discordance response to HAART.

2.2. Study area, design, and population

A hospital-based cross-sectional study with secondary data review was conducted among HIV positive individuals on HAART from February 1 to May 30, 2017, in the HIV Care Unit at the University of Gondar Referral Hospital (UOGRH) Gondar, Ethiopia. All Adult HIV positive individuals who received HAART in the HIV Care Unit at UOGRH were the study population.

Those HIV positive individuals aged 18 years or older (adult) who was being on HAART for more than 6 months, and CD4+ cell counts with a minimum of 2 separate measurements over the previous 6 months; visited and consented to be involved in HIV Care Unit at UOGRH during the study period were included in the study.

But, patients who unable to give the response because of seriously sick, having taken part in the HAART discontinuation program at any time during follow-up, having undergone treatment with interferon or chemotherapy during the preceding year, irregular or interruption use of HAART over the previous year, failure to attend the clinic in the previous 6 months; being pregnant at the time of the sampling and patients with an incomplete laboratory and clinical data, such as adherence, drug regimen, HIV/AIDS World Health Organization (WHO) stage, weight, etc were excluded from the study.

2.3. Sample size determination and sampling technique

Since similar study has not been done previously, 430 sample size including 15% nonresponse rate was calculated by considering the following assumptions, P = population proportion (estimated prevalence) = 0.5, precision d, 0.05, assuming 95% confidence interval $\alpha = 0.05$ and z (1–a/2) = 1.96.

Study participants were selected using a systematic random sampling technique. One thousand eight hundred HIV positive individuals on HAART were expected to visit the HIV care unit of the hospital during the 4-month data collection period for follow-up. The average number of HIV positive individuals per day under follow-up in the HIV care unit was 15. Sampling intervals (K value = 4) was calculated with 1800/430 = 4.18 = 4. Thus data collection (interviews, chart review, and blood (for CD4+ count and VL) were conducted at 4 intervals. Lottery method was done to determine the first study participant at the 1st day from 15 patients who had been under follow-up and then each 4th client was selected for data collection (interviews, chart review, and blood (for CD4+ count and VL). If the 4th patient is not fulfilling the inclusion criteria; the next person was taken as a study participant (Fig. 1).

2.4. Data collection and laboratory methods

Socio-demographic characteristics and clinical data (age, gender, residence, education, occupation, VL, CD4+ count, co-infections, adherence at base line, baseline CD4+ count, regimen type, WHO stage, duration of follow-up time, adherence during data collection, etc) were collected by interview and from the patient individual chart by trained nurses using a semi-structured questionnaire.

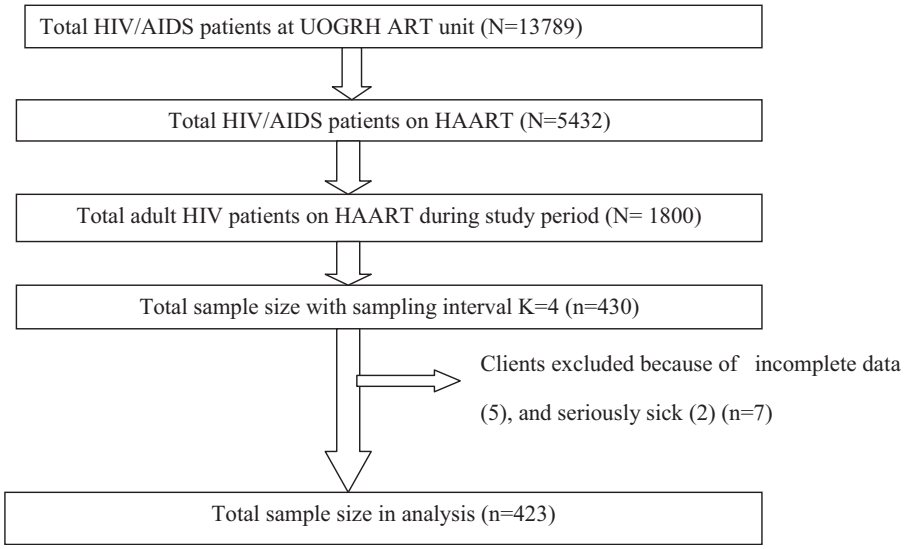

Figure 1. Schematic representation of the sampling procedure of adult HIV positive individuals on HAART at UOGRH from February 1 to May 30, 2017. 13,789 = the total number of HIV positive individuals who visited UOGRH ART unit, 5432 = the total number of HIV positive individuals on HAART at UOGRH ART unit, 1800 = HIV positive individuals on HAART who visit UOGRH during data collection period (February 1 to May 30, 2017), 430 = total sample size with sampling interval K = 4, 423 = sample sizes used for analysis by excluded 7 study participants, ART = antiretroviral therapy, HAART = highly active antiretroviral therapy, HIV = human immune deficiency virus, UOGRH = University of Gondar Referral Hospital.

About 10 mL venous blood was collected from each patient for CD4+ and VL test using vacutainer tube containing anticoagulant ethylene diamine tetra-acetic acid following blood collection standard operational procedure (SOP). After collection 3 to 5 mL of 10 mL of blood was centrifuged (3000 rpm for 20 minutes), and plasma was separated for VL testing. The remaining blood sample (3–5 mL) was used for CD4+ T cell count. During specimen collection, labeling, transportation, storage (CD4+ T cell count = 20–25 °C, VL = −80 °C), and analysis (CD4+ T cell count and VL) was done following the SOP of the laboratory. Specimen for CD4+ T cell count was tested within 24 hours and specimen for VL testing was done within 5 hours after plasma was separated. Centrifugation, pipetting, and aliquoting were performed following laboratory SOP, and laboratory bio-safety precautions both at the collection and testing site.

Quantification of CD4+ T cell count on whole blood specimen was done using the FACSCalibur flow cytometry (BD, CA) by adding 50 μL whole blood to a reagent tube containing 20 μL of monoclonal antibodies followed by vertexing and incubation for 30 minutes under dark condition. Whereas, plasma VL was measured using Quantitative Real-Time PCR HIV-1 assay by the COBAS AmpliPrep instrument (Roch, Homburg, Germany) by preparing plasma from 5 mL of blood according to SOP.

2.5. Variables' definition

Virological response: A confirmed HIV RNA level below the lower limit of detection available assays[8,9] so in our assay it is defined as HIV RNA plasma VL of a patient achieving a plasma VL of undetectable level or ≤20 cp/mL after 6 months on HAART.

Immunological response: is defined as an increase of 50 CD4+ cells/mm3 of a patient after 6 months on HAART.[10]

Virological discordant: is defined as above the limit of detection of the assay or ≥ 20 cp/mL after 6 months on treatment.[9]

Immunological discordant: is defined as CD4+ cells count < 50 cells/μL after 6 months on HAART.[10]

Adherence: Adherence was calculated as number (No) of the dose of HAART taken/No of prescribed doses of HAART × 100%. Good adherence, >95%, fair adherence, 85% to 95% and poor adherence, <85% doses take.[11]

2.6. Study variables

Dependent variables: Virological discordant for ART and immunological discordant for HAART.

Independent variables: Age, sex, residence, education, occupation, HIV/AIDS co-infection, base line and current CD+ count, regimen type WHO stage, and duration of follow-up time, etc.

2.7. Data processing and analysis

After checking the completeness of the data, it was entered into SPSS version 20 for analysis of descriptive (percentage, mean, and standard deviation), bivariate and multivariate logistic regression. Bivariate logistic regression was done to assess the crude association between independent and dependent variables with a *P*-value ≤ .20 whereas, multivariate logistic regression was done to identify statistically significant (*P*-value < .05) independent predictors for virological and immunological discordance.

3. Results

3.1. Socio-demographic characteristics of study participants

A total of 423 HIV positive individuals who initiate HAART at the UOGRH were included in the analyses. The mean age of the patients at study time was 39 (± 9.8) years (range 18–78 years) and the majority of the patients were female (n = 269; 63.6%). Three hundred forty (80.4%) were living in urban areas (Table 1).

Table 1

Socio-demographic characteristics of HIV/AIDs patients on HAART at the University of Gondar Referral Hospital, 2017.

Variables		Frequency (%)
Age	18 to 29	52 (12.3)
	30 to 39	171 (40.4)
	40 to 49	139 (32.9)
	≥50	61 (14.4)
Marital status	Single	97 (22.9)
	Married	209 (49.4)
	Divorced	81 (19.1)
	Widowed	36 (8.5)
Gender	Female	269 (63.6)
	Male	154 (36.4)
Resident	Urban	340 (80.4)
	Rural	83 (19.6)
Occupation	Government employ	43 (10.2)
	Merchant	56 (13.2)
	Farmer	51 (12.1)
	Student	16 (3.8)
	House life	104 (24.6)
	Daily laborer	62 (14.7)
	Private employ	65 (15.4)
	Other	26 (6.1)
Educational status	Illiterate	142 (33.6)
	Primary school	121 (28.6)
	Secondary school	117 (27.7)
	Tertiary	43 (10.2)
Religion	Orthodox	390 (92.2)
	Muslim	31 (7.3)
	Protestant	2 (0.5)
	Total	423 (100.0)

AIDS = acquired immune deficiency syndromes, HAART = highly active antiretroviral therapy, HIV = human immune deficiency virus.

3.2. Clinical characteristics of HIV positive individuals

The average follow-up duration of patients on HAART was 7 (±3) years (range 0.5 up to 12 years). Before HAART initiation majority of patients were have WHO clinical stage of II and III (n = 311; 73.5%), were have CD4+ T cell count < 200 cells/mm^3 (n = 267; 63.1%) and were had good adherence (n = 408; 96.5%). Whereas at the time of data collection time 419 (99.1%) had WHO clinical stage of I and II, 379 (89.6%) had CD4+ T count ≥ 200 cells/mm^3, 420 (99.3%) had good adherence, 308 (72.8%) patients were had undetectable VL, 162 (38.2%) patients were switched to either first-line or second-line drug, and toxicity 109 (67.3%) was the most common reason for switching drug (Table 2).

3.3. Overall discordant

Four hundred twenty-three participants were followed for a different period and the total person–time of follow-up was 3026 patient–years of follow-up. Hence, the rate of immunological and virological discordance for HAART drugs was 1.9 and 6.7 patients per year of follow-up, respectively. Out of 423 HAART patients, 221 (52.2%) had either immunological or virological discordant, 56 (13.2%) had an immunological discordance, 199 (47%) had virological discordance and 34 (8%) had both immunological and virological discordance to HAART drug (Table 3).

3.4. Immunological discordant and associated factors

In bivariate logistic regression analysis associated factors, such as the duration on HAART, opportunistic infection, and VL during data collection were found to be a *P*-value of <.2. When it was analyzed with multivariate logistic regression analysis, the duration of follow-up on HAART ≤6 years, and VL ≥ 20 copies/mm^3 were significant factors ($P < .001$) for immunologic

Table 2

Clinical characteristics of HIV/AIDs patients on HAART at the University of Gondar Referral Hospital, 2017.

Variables		Frequency (%)
Duration of ART in year	≤6	162 (38.3)
	>6	261 (61.7)
Base line WHO stage	WHO stage I	57 (13.5)
	WHO stage II	97 (22.9)
	WHO stage III	214 (50.6)
	WHO stage IV	55 (13.0)
WHO stage during data collection	WHO stage I	11 (2.6)
	WHO stage II	408 (96.5)
	WHO stage III	4 (.9)
Type of opportunistic infection	No	308 (72.8)
	Protozoa	4 (.9)
	Helminths	12 (2.8)
	Hepatitis viruses	3 (.7)
	Fungal infections	1 (.2)
	TB	89 (21.0)
	Mixed	6 (1.4)
Initial regimen	D4T + 3TC + NVP	78 (18.4)
	D4T + 3TC + EFV	29 (6.9)
	AZT + 3TC + NVP	156 (36.9)
	AZT + 3TC + EFV	30 (7.1)
	TDF + 3TC + EFV	87 (20.6)
	TDF + 3TC + NVP	31 (7.3)
	D4T + 3TC + NVP	6 (1.4)
	Pediatric 4C (AZT + 3TC + NVP)	6 (1.4)
Switching	No	261 (61.7)
	Yes	162 (38.3)
	Total	423 (100.0)
Switching	To 1st line drug	150 (35.5)
	To 2nd line drug	12 (2.8)
Second regimen	AZT + 3TC + NVP	61 (37.7)
	AZT + 3TC + EFV	25 (15.4)
	TDF + 3TC + NVP	25 (15.4)
	TDF + 3TC + EFV	39 (24.1)
	ABC + ddI + LPV/R	11 (6.8)
	TDF + ddI + IPV/R	1 (.6)
Reason of switching drug	Toxicity	109 (67.3)
	Pregnancy	7 (4.3)
	TB	18 (11.1)
	Clinical failure	1 (.6)
	Age	9 (5.6)
ARV drug ADH at base line	Good	408 (96.5)
	Fair	2 (.5)
	Poor	13 (3.1)
ARV drug ADH during data collection	Good	420 (99.3)
	Poor	3 (.7)
Base line CD4 count	<200	267 (63.1)
	≥200	156 (36.9)
CD4 count during data collection	<200	44 (10.4)
	≥200	379 (89.6)
Viral load count	Undetected	308 (72.8)
	>20	115 (27.2)
	Total	423 (100)

ABC = abacavir, ADH = adherence, AIDS = acquired immune deficiency syndromes, ART = antiretroviral therapy, ARV = antiretroviral, AZT/3TC = zidovudine/lamivudine, D4T = stavudine, ddI = didanosine, EFV = efavirenze, HAART = highly active antiretroviral therapy, HIV = human immune deficiency virus, LPV/R = lopinavir/ritonavir, Mixed = patients infected with more than 2 organisms, NVP = nevirapine, TDF = tenofovir disoproxil fumarate, WHO = World Health Organization.

Table 3

Magnitude of immunological and virological discordant to ART among patients on HAART at the University of Gondar Referral Hospital 2017.

		Virological discordant to ART		
		No	Yes	Total
Immunological discordant to ART	No	202 (47.8%)	165 (39%)	367 (86.8%)
	Yes	22 (5.2%)	34 (8%)	56 (13.2%)
Total		224 (53%)	199 (47%)	423

ART = antiretroviral therapy, HAART = highly active antiretroviral therapy.

discordant. Patients with a duration follow-up on HAART ≤ 6 years (adjusted odds ratio [AOR] = 3.29 [1.80–6.03], $P = .001$) and VL ≥ 20 (AOR = 3.08 [1.70–5.61], $P < .001$) were 3.29 and 3.08 times more likely to have immunological discordance for HAART compared with those comparison >6 years of follow-up and patients those have had undetectable VL, respectively (Table 4).

3.5. Virological discordant and associated factors

From the bivariate analysis, HAART drug type, CD4 count during data collection, and drug switching as a result of TB co-infection, immunological failure, default, and age were had a *P*-value of <.2. But multivariate regression analysis showed only patients who switched drug as a result of TB co-infection was significant factors ($P \leq .05$) for virological discordance. The patients who switched drugs as a result of TB co-infection (AOR = 3.33 [1.10–10.08]), $P = .03$) was 3.33 times more likely to have virological discordance of HAART compared with their comparison group who switched drug as a result of toxicity (Table 5).

4. Discussion

This study assessed the prevalence of immunological and virological discordance and their associated factors. The finding of the study revealed a high frequency of immunological and virological discordance, and the related risk factors for immunological discordance was being on the duration of follow-up, being on HAART ≤ 6 years and had VL ≥ 20 copies/mm^3, whereas for virological discordance was patients who switched drug as a result of TB.

In our study, the prevalence of discordant immunological response (13.2%) was consistent with studies conducted in Europe 12%, 15%.[12,13] But lower than studies conducted in South Africa 24%, 37%,[14,15] Nigeria 22.6%,[16] France 20% to 40%,[17] and Tanzania 50.25%.[18] The prevalence variation was due to the difference in CD4+ cell count cutoff value which defines immunologic nonresponse. In our study, the definition of the discordant immune response was derived from the National Institutes of Health guidelines which defined an inadequate immunological response to HAART as an increase in CD4+ count < 50 cells/μL per year after 6 months of follow-up on HAART.[2,17–19] But in other study immunologic nonresponse was defined based on the considerations of the increase in CD4+ count overtime since the start of HAART in virologically suppressed patients depends on baseline CD4+ count and the risk of mortality which is strongly related to current CD4+ count.[12–18,20]

Our study showed that being within the duration of follow-up on HAART ≤6 years ($P \leq .001$) was significantly associated with the discordant immunological response with HAART. This finding was agreed with the previous study conducted in Ethiopia[17] and Malaysia.[21] But, it has disagreed with the study done in Ethiopia.[22] The discrepancy might be due to the lack of assessment of drug resistance virus from HIV positive individuals who had acquired drug resistance virus from patients who were not on HAART for a long duration to exclude from the study.

In our study VL ≥20 copies/mm^3 ($P \leq .001$) was the other significant factor for the discordant immunological response. This finding was agreed with the findings of other studies conducted in Ethiopia[21,23,24] and Eurosids.[25] Even though there is no direct relationship between CD4+ count and VL, during treatment, a high CD4+ count and a low or undetectable VL are desirable. The higher the CD4+ counts the healthier the immune system. The lower the VL, the expected HIV therapy is being worked. On the other hand, if the treatment is not effective,

Table 4

Bivariate and multivariate analysis of associated risk factors of immunological discordance to ART on ART/AIDs patients attending the University of Gondar Referral Hospital 2017.

		Immunological discordance to ART					
Variables		Yes	No	*P*-value	COR (95%CI)	AOR (95%CI)	*P*-value
Duration on ART in year	≤6	36	126	.0001	3.44 (1.91–6.19)	3.29 (1.80–6.03)	**.0001**
	>6	20	241		Ref	Ref	
Opportunistic infection	Yes	8	107		Ref	Ref	
	No	48	260	.023	2.47 (1.13–5.40)	2.08 (0.93–4.67)	.075
Viral load (copies/mm^3)	Undetectable	29	279		Ref	Ref	
	≥20	27	88	.0001	2.95 (1.66–5.25)	3.08 (1.70–5.61)	**.0001**

AIDS = acquired immune deficiency syndromes, AOR = adjusted odds ratio, ART = antiretroviral therapy, CI = confidence interval, COR = crude odds ratio, HAART = highly active antiretroviral therapy, *P* = significant value, Ref = reference.

*Has significant association.

Table 5

Bivariate and multivariate analysis of associated risk factors of virological discordance to ART among patients on HAART at the University of Gondar Referral Hospital 2017.

Variables		Virological discordance to ART		*P*-value	COR (95%CI)	AOR (95%CI)	*P*-value
		Yes	No				
ART d drug	Efavirenze	69	89		Ref	Ref	
	Nevirapine	120	132	.435	1.17 (0.79–1.75)	2.09 (0.95–4.60)	.06
	second line	10	3	.031	4.30 (1.14–16.22)	14.05 (0.76–259.95)	.07
CD4 count during data collection	<200	34	10	.0001	4.41 (2.12–9.19)	1.75 (0.511–5.99)	.37
	≥200	165	214		Ref	Ref	
Reason of switching drug	Toxicity	47	61		Ref	Re f	
	Pregnancy	3	4	.973	0.97 (0.21–4.56)	0.81 (0.17–3.92)	.80
	TB	12	7	.12	2.23 (0.81–6.09)	3.33 (1.10–10.08)	.03
	Immunological failure	9	4	.09	2.92 (0.85–10.07)	0.45 (0.03–6.48)	.55
	Default	6	1	.06	7.79 (0.91–66.91)	7.20 (0.82–63.55)	.07
	Age	7	1	.04	9.09 (1.08–76.41)	6.31 (0.73–54.82)	.09

Those variables with in *P* value <.2 under bivariate analysis were included with in multivariate analysis.

AOR = adjusted odds ratio, ART = antiretroviral therapy, Ref = reference CI = confidence interval, COR = crude odds ratio, HAART = highly active antiretroviral therapy, *P* = significant value.

*Has significant association.

VL: increases, invades, and turns healthy CD4+ cells into factories of new copies of HIV and destroyed them. As a result, CD4+ count may be decreased even though the patient is on HAART and the VL may also increase.

The prevalence of virological discordant to HAART in our study (47%) was consistent with the study conducted in Colombia, Canada with an estimated range of 56.7% to 70.1%.[26] However, our result was higher compared to findings of certain systematic reviews 7%, 22%, 39%[21,27,28] the study conducted in Ethiopia 11% and 26.4%,[22,29] in Uganda 11%,[15] in Nigeria 23.3%,[30] in South Africa 15%, 28%,[31,32] African cohort study 9%,[33] Nepal 9.92%,[34] and Netherlands 23%.[35] The difference in prevalence might be because of the difference in the types of VL assays, in the definition of virological nonresponse, and in the cutoff point. Our study used an assay which considered greater >20 copies/mm^3 for the definition of virological nonresponse and for the cutoff point. But other studies was used >50 copies/mL and 400 copies/mL.

In the current study, co-infection with TB was a significant factor for discordant virological response to HAART. The finding is in line with a study conducted in South African,[30,36] and Uganda[37] but not consistent with a previous study conducted in Ethiopia.[38] This could be due to the concurrent HAART and TB drug treatment. Particularly, due to impaired treatment adherence, and pharmacokinetic drug interaction.

5. Limitation

There are some limitations in our study that can be the potential bias, the first one is a drug resistance test that was not done due to lack of laboratory set up and the other was VL of HIV positive individuals at the baseline after 6 months of HAART not performed since VL assay was started in Ethiopia after 2016.

6. Conclusion

The virological discordance to HAART and immunological discordance to HAART was high which makes it less likely to achieve the third UNAIDS 90 target. Being within the ≤6 years duration of follow-up on HAART and having VL ≥ 20 copies/mm^3 were significantly associated with immunological discordance to HAART. Whereas, co-infection with TB during receiving HAART service were significantly associated with virological discordance to HAART. Hence, intensive adherence support and counseling should be provided to achieve the UNAIDS 90 target. HIV positive individuals who encountered co-infection with TB, who have had VL ≥ 20 copies/mm^3, and who are ≤6 years duration of follow-up on HAART need to be carefully monitored. In addition, a national-based study including the genetic sequencing of this discordant group is needed.

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