Outcomes and Determinants of Treatment Adherence among HIV Patients on Art: Evidence from a Retrospective Cohort Study in Selected Clinics in Windhoek, Namibia

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Abstract

Background: Treatment adherence is critical in the management of patients receiving antiretroviral therapy (ART).

Objective: To investigate determinant of treatment adherence and health-related outcomes after ART initiation in Windhoek, Namibia.

Methods: We used data from retrospective cohort from January 2010 to December 2015. We defined ART adherence at ≥95%, while non-adherence at <95% . We examined two outcomes: viral suppression and body weight at 6 and 12 months.. We then investigated the relationship between patient individual outcomes and treatment adherence. We applied multivariate binary and multinomial logistic regression models to examine the determinants of ART adherence and outcomes.

Results: Of 943 patients on ART, 58.9% were female, 82.1% aged between 25 to 49 years old and 86.6% ever married. Viral suppression at 6 months (p<0.000), and 12 months (p<0.000), and patients' body weight at 6 months (p = 0.009) were significant more pronounced with ART adherence.. Regarding determinants of ART adherence, the results showed age between 25 and 29 years, and married was associated with higher adherence (OR=1.94, CI: 1.12-3.14). Patients at WHO clinical stage-I were more likely to adhere to treatment (OR=1.28, 95% CI: 1.01-1.73), while those at clinical stage-II were less likely (OR=0.41, 95% CI: 0.18-0.91, p-value = 0.028).

Conclusion: ART adherence leads to better outcomes.. Both demographic and clinical factors were associated with ART adherence. Future research should consider evaluating the effect of adherence to an extended coverage of clinics, and allow collecting more detailed factors that are associated with treatment adherence.

Keywords: HIV; Antiretroviral Therapy; ART adherence; viral suppression; multinomial logistic regression.

Introduction

Human immunodeficiency virus (HIV) epidemic has become one of the major challenges to public health care sector worldwide. According to 2017 World Health Organization (WHO), more than 70 million people have been infected with the HIV virus and about 35 million people have died of HIV attributable illness. Globally, 36.7 million people were living with HIV at the end of 2016, with an estimated 0.8% of adults aged 15 to 49 years worldwide affected. Although the burden of the epidemic continues to vary considerably between countries and regions, the sub-Saharan Africa remains the most severely affected, with nearly 1 in every 25 adults (4.2%) living with HIV and accounting for nearly two-thirds of people living with HIV worldwide (WHO, 2017). In Namibia, the proportion of people presenting with HIV infection has remained largely unchanged during 2010 to 2015 years.

In 2015, the Joint United Nations Program on HIV and AIDS (UNAIDS) developed the 90-90-90 targets to be achieved by 2020 with the aim of eliminating AIDS epidemic globally by 2030 (MoHSS, 2016). In order for the country to eliminate the HIV epidemic, health practitioner need to test 90% of all the people who are estimated to be HIV positive and let them know their status, assess antiretroviral therapy (ART) to 90% of all those who test HIV positive and retain them on ART so that 90% of all those on treatment have viral load suppressed by 2020. Therefore, the achievement of

the 90-90-90 target in 2015 globally was around 11.9 million people living with HIV who did not know their HIV status, 12.7 million people in need of antiretroviral treatment and 13.0 million people living with HIV who were not virally suppressed (UNAIDS, 2016). In Namibia, 77% of people were estimated HIV positive and know their HIV status, 64% of people living with HIV are on treatment and all those who were virally suppressed they have not been identified (UNAIDS, 2016).

The Namibia National Policy on HIV/AIDS 2007, together with National Strategic Framework for HIV and AIDS, highlights the need of giving HIV care to people living with HIV and their families, and includes HIV prevention, diagnosis, treatment, and care and support services (Ministry of Health and Social Services [MoHSS], 2016). In 2003, the government of Namibia introduced provision of free antiretroviral therapy (ART) to the public. According to MoHSS (2017), since the roll-up of ART, 93% of HIV patients that have been enrolled into the ART program and they are living healthy lives thus contributing to the economy of the country (MoHSS, 2016). Although the number of people receiving ART has increased (UNAIDS, 2017), very little is known on the achievement of optimal levels of 90-90-90, particularly on adherence.

To achieve such optimal levels, requires continuous treatment adherence. However, a number of studies have shown that non-adherence is a major issue and a rising problem (Heestermans et al., 2016; Kheswa, 2017). There is need to understand factors associated with adherence or non-adherence to enable redesigning health promotions.

The World Health Organization (WHO) defined adherence as the extent to which a person's behavior corresponds with the agreed recommendations of a healthcare provider. Although, adherence behavior is influenced by the clinician and the healthcare system, the disease and its treatment it can also influenced by economic and social factors (Noens et al., 2009). Adherence to antiretroviral therapy (ART) is essential to ensure viral load suppression, decrease the risk of disease progression and drug resistance (Rougemont, Stoll, Elia & Ngang, 2009). However, sustaining adherence to ART over the long term requires accurate and consistent monitoring. In particular, according to Nachega, Mills and Schechter (2010), and Reda and Biadgilign (2012), sustaining adherence to ART is a challenge for countries in sub-Saharan Africa. Moreover, despite many studies elsewhere, there are no published results on outcome and determinants of treatment adherence in Namibia.

The paper, therefore, reports on a study designed to examine treatment adherence outcomes among HIV-patients on ART treatment in Namibia. Specifically, the objective was to compare the health-related outcomes by ART treatment adherence and to explore factors associated with the outcomes i.e. viral load suppression and weight at ART both 6 months and 12 months, as well as those factors related to treatment adherence. We first compare the outcomes by the determinants of treatment adherence among HIV patients on ART. We then examined the relationship between with patient individual outcomes and treatment adherence.

Methods

Study sites

Two health facilities, Katutura Health Center and Okuryongava Clinic, in Windhoek were selected for evaluation. The two clinics form part of the public health care services in Windhoek, the capital city of Namibia. In total, Namibia has 343 health care centres, of these only seven public clinics are in Windhoek (i.e the Khomasdal, Robert Mugabe, Donkerhoek, Black chine, Wanaheda, Okuryangava and Hakahana clinics). Since this study was an evaluation assessment, only two facilities were selected. These facilities provide free HIV care, including counselling and give ART medications for free.

Study design

The design was a quantitative retrospective cohort study design. The data were collected among the patients who initiated ART from January 2010 to December 2015 at Katutura Health Centre (KHC) and Okuryangava Clinic (OC). The target age group was all patients aged 16 years and above.

Sample size and sampling

The sample size was estimated at 942 under the following assumption; (1) to detect a relative risk of 2 between the exposed and non-exposed; (2) two-sided significance of 95%; a power of 80%, ratio

of sample equal to 1 between the exposed (less than 95% adherence to ART) and un-exposed (at least 95% adherence to ART) and (3) percent of unexposed with outcome equal to 5% and percent of exposed with outcome equal to 10%. The sample was selected from two health facilities using the following approach: First the simple random sampling of the patients' files was done, followed by a systematic sampling whereby every third file was selected until the desired sample was achieved. An equal sample was planned for each clinic, however, Okryangava was oversampled as it had more patients.

Eligibility and ineligibility criteria

Included all HIV patients ever started on ART between January 1, 2010 to December 31, 2015 and aged 16 to 50 years, and excluded all those that did not meet this criteria.

Variables

In this context, two health outcomes were considered. The primary outcome was the viral load suppression, and the secondary outcome was body weight. Both were evaluated at 6 months and 12 months after the ART initiation. Another potential outcome was CD4 count, however, this was not recorded at 6 and 12 months after initiating ART. Treatment adherence was the main effect modifier. Treatment adherence was defined as those who achieved at least 95% adherence to ART, and non-adherence if there was less than 95% inconsistent uptake of ART. The covariates included were age, sex, marital status, facility, WHO stage, ART regimens and hepatitis B.

Data analyses

In preliminary analyses, patient's outcomes such as viral load suppression and weight at 6 months and 12 months were compared by whether they adhered to ART treatment or not, and used Pearson Chi-square test for statistical significance. In the analyses of ART adherence, multivariate logistic regression was used to assess the associations between factors and the outcomes by comparing odd ratios (OR), the corresponding 95% confidence interval (CI), and p-value. Further analyses, consider multinomial logistic regression to examine if there is an association between factors and patients' body weight 6 and 12 months. A two sided p-value below 0.05 level of significance was considered statistically significant. All analyses were performed using SPSS version 22.

Ethical clearance

The approval was obtained from the Research Ethical Committees of Texila American University and the Ministry of Health and Social Services of the Republic of Namibia.

Results

Table 1 shows the sample characteristics of all HIV patients on antiretroviral therapy in selected health facility in Namibia. A total of 943 patients (45.6% from KHC and 54.4% from OC) were included in the study. Of these, 555 (58.9%) were female and 388 (41.1%) were male. The highest age group was 773 (82.1%) age between 25 to 49 years old as compare to other age group. The majority of the sample were 783 (86.6%) ever married.

Table 1. Sample characteristics of HIV patients on antiretroviral therapy in selected health facility in Namibia

Variables	n	%
Facility		
Katutura hospital center (KHC)	430	45.6
Okuryangava clinic (OC)	513	54.4
Sex		
Male	388	41.1
Female	555	58.9
Age group (years)		
< 25 years	129	13.7
25-49 years	773	82.1

≥ 50 years	40	4.2
Marital Status		
Single	783	86.6
Married	115	12.7
Others	6	0.7
Adherence		
Yes	651	69.1
No	291	30.9

Note: "n" denote the number of HIV patients and "%" the percentage of HIV patients.

About 69.1% (n=651) patients were classified as to have adhered to ART (Table 1). Figure 1 shows the percentage of HIV patients of health-related outcomes disaggregated by ART adherence. The figure revealed that patients whose viral load was suppressed at 6 months, 77.8% adhered to treatment, while at 12 months, those whose viral load was suppressed, 89.4% adhered to treatment.

Figure 1. The percentage of HIV patients of health-related outcomes (viral load suppression and weight) by ART adherence
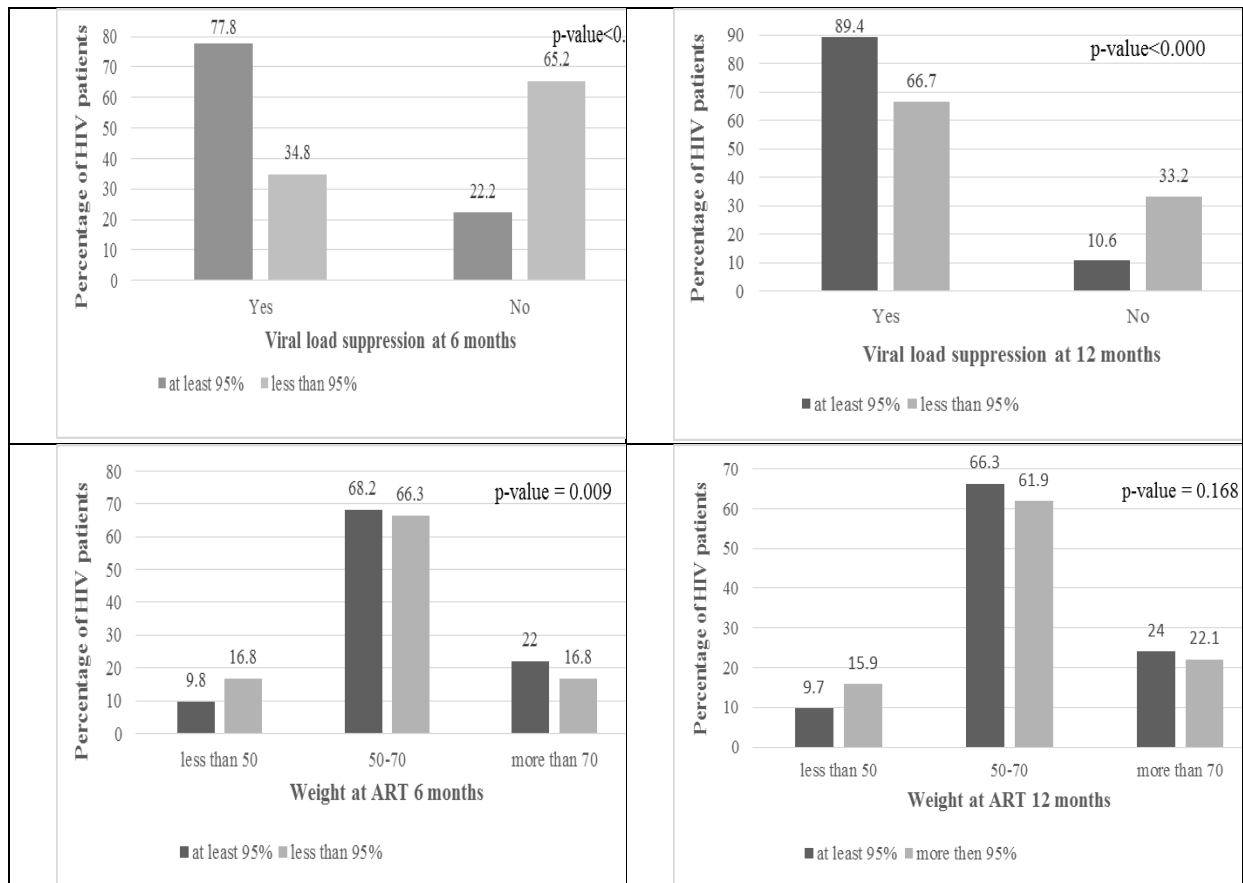

Table 2 presents the relationship between ART adherence and health related outcomes: patients' viral load suppression and patients' body weights both at 6 months and 12 months. The results revealed that viral load suppression at both 6 and 12 months were statistically significant with ART treatment adherence (p-value<0.000). The results also revealed that patients' body weight at 6 months (p-value = 0.009) was statistically significant at 5% level of significance. On the other hand, patients' body weight at 12 months was not statistically significant with ART treatment adherence (p-value =0.168). This suggests there was not much change in body weight between 6 and 12 months.

Table 2. Relationship between adherence level and patients' viral load suppression at 6 months and 12 months and weight at 6 months and 12 months on ART

Variables	Adherence		P-value
	at least 95%	less than 95%	
Viral load suppression at 6 months	%	%	p<0.000
Yes	77.8	34.8	
No	22.2	65.2	
Viral load suppression 12 months			p<0.000
Yes	89.4	66.7	
No	10.6	33.2	
Weight at ART 6 months			p = 0.009
less than 50	9.8	16.8	
50-70	68.2	66.3	
more than 70	22	16.8	
Weight at ART 12 months			p = 0.168
less than 50	9.7	15.9	
50-70	66.3	61.9	
more than 70	24	22.1	

Table 3 presents the results of multivariate binary logistic regression. Regarding ART adherence, the results show that patients aged between 25 and 29 years, compared to those of age 50 years and above, were more likely to adhere to treatment (OR=1.29, 95% CI:106-2.18). Similarly being married was associated with higher adherence (OR=1.94, CI: 1.12-3.14). Patients at WHO clinical stage-I were more likely to adhere to treatment (OR=1.28, 95% CI: 1.01-1.73), while those at clinical stage-II (OR=0.41, 95% CI: 0.18-0.91, p-value = 0.028) were less likely to be associated with ART treatment than patients at clinical stage-IV. Patients who were at clinical stage-III were marginally significant (p-value = 0.054). The results further show that, based on OR only, ART regimen showed higher likelihood towards adherence, nevertheless, these were not significant.

Table 3. Multivariate odd ratios (OR) of the association between factors and the outcomes i.e. viral load suppression at 6 months and viral load suppression at 12 months and ART adherence

Factors	ART adherence		Viral load suppression at 6 months		Viral load suppression at 12 months	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Age group (ref. >50)						
25-49	1.29 (1.06, 2.18)	0. 02	1.29 (0.56, 3.04)	0.55	0.61 (0.12, 3.21)	0.55
>50	0.88 (0.42, 1.85)	0.74	1.01 (0.48, 2.12)	0.99	1.33 (0.36, 4.87)	0.67
Sex (ref. female)						
Male	0.82 (0.60, 1.12)	0.21	0.81 (0.59, 1.11)	0.21	1.27 (0.73, 2.20)	0.39
Marital Status (ref. others)						
Single	0.96 (0.29 , 3.11)	0.95	1.03 (0.15, 6.96)	0.98	1.11 (0.14, 8.93)	0.92
Married	1.94 (1.12, 3.14)	0.01	1.12 (0.16, 7.77)	0.91	1.16 (0.14, 9.59)	0.89
Clinical stage (ref. stage-IV)						
stage-I	1.28 (1.01, 1.73)	0.03	0.30 (0.12, 0.75)	0.01	0.19 (0.05 , 0.83)	0.03
stage-II	0.41 (0.18, 0.91)	0.03	0.26 (0.09, 0.75)	0.01	0.32 (0.07, 1.59)	0.17
stage-III	0.41 (0.17, 1.02)	0.05	0.46 (0.17, 1.26)	0.13	0.35 (0.07, 1.66)	0.15
Hepatitis B (ref. negative)						
Positive	0.64 (0.27, 1.53)	0.31	1.06 (0.65, 1.71)	0.83	0.89 (0.35, 2.26)	0.81
ART regimen (ref. others)						
TDF/FTC/EFV	1.12 (0.49, 2.52)	0.79	0.54 (0.22, 1.33)	0.18	0.28 (0.08, 0.98)	0.04
TDF/3TC/EFV	1.04 (0.47, 2.29)	0.93	0.67 (0.28, 1.62)	0.38	0.52 (0.16, 1.69)	0.27
TDF/3TC/NVP	1.03 (0.46, 2.30)	0.95	0.60 (0.25, 1.48)	0.27	0.66 (0.19, 2.21)	0.49

Note: TDF = tenofovir, FTC = emtricitabine, EFV = efavirenz, 3TC = lamivudine, NVP = nevirapine, OTHER = zidovudine (AZT) and stavudine (d4T).

With regards to viral load suppression at both 6 months (Table 3), patients who were at clinical stage-I (OR=0.30, 95% CI 0.12-0.75, p-value = 0.010) and stage-II (OR=0.26, 95% CI 0.09-0.75, p-value = 0.010) were less likely to be associated with viral load suppression at 6 months. Similarly, viral load suppression at 12 months was associated with clinical stage. Patients at clinical stage-I (OR=0.19, 95% CI 0.05-0.83, p-value = 0.027), and those treated with a combination ART regimen containing tenofovir (TDF), emtricitabine (FTC) and efavirenz (EFV) (OR= 0.28, 95% CI 0.08-0.98, p-value = 0.04) were less likely to be associated with viral load suppression at 12 months (Table 3).

Table 4. Multinomial odd ratios (OR) of the association for patients' body weight at 6 months

Factors	Weight at 6 months of ART			
	Less than 50 kg		Between 50 to 70 kg	
	OR (95% CI)	P-values	OR (95% CI)	P-values
Age group (ref. >50)				
<25	1.63 (0.35, 7.54)	0.53	1.04 (0.34, 3.13)	0.95
25-49	0.77 (0.19, 3.02)	0.71	0.95 (0.37, 2.43)	0.91
Sex (ref. female)				
Male	0.34 (0.18, 0.64)	0.001	0.85 (0.58, 1.25)	0.43
Facility (ref: OC)				
KHC	0.91 (0.51, 1.63)	0.75	1.06 (0.73, 1.56)	0.73
WHO stage (ref. stage-IV)				
stage-I	0.58 (0.09, 3.66)	0.56	0.66 (0.18, 2.38)	0.52
stage-II	0.66 (0.08, 5.23)	0.69	0.96 (0.24, 3.88)	0.94
stage-III	1.96 (0.26, 14.91)	0.51	1.57 (0.36, 6.72)	0.54
Hepatitis B (ref. negative)				
Positive	1.06 (0.43, 2.59)	0.89	0.82 (0.46, 1.46)	0.50
ART regimens (Others)				
TDF/FTC/EFV	0.09 (0.01, 0.87)	0.04	0.25 (0.03, 1.97)	0.18
TDF/3TC/EFV	0.08 (0.01, 0.73)	0.02	0.19 (0.02, 1.49)	0.11
TDF/3TC/NVP	0.08 (0.01, 0.76)	0.03	0.22 (0.03, 1.74)	0.15

The reference category: more than 70 kg weight.

Regarding patients' body weight at 6 months of ART (Table 4), male patients (OR: 0.34, 95% CI: 0.18-0.64, p-value = 0.001) and those who received combination of ART regimens containing tenofovir (TDF), emtricitabine (FTC) and efavirenz (EFV) (OR= 0.09, 95% CI 0.01-0.87, p-value = 0.037), tenofovir (TDF), lamivudine (3TC) and efavirenz (EFV) (OR: 0.08, 95% CI: 0.01-0.70, p-value = 0.023) and tenofovir (TDF), lamivudine (3TC) and nevirapine (NVP) (OR= 0.08, 95% CI 0.01-0.76, p-value = 0.028) were less likely to be associated with body weight of less than 50 kg. Age, sex, facility, WHO stage, hepatitis B and ART regimens were not statistically significant with patients' body weight of 50 to 70 weights (Table 4).

Determinants of body weight at 12 months are given in Table 5. Again being male (OR=0.39, 95% CI: 0.20-0.76, p-value = 0.005) were less likely to be associated with those who were less than 50 weight. The ART regimens containing tenofovir (TDF), lamivudine (3TC) and nevirapine (NVP) (p-value = 0.054), tenofovir (TDF), emtricitabine (FTC) and efavirenz (EFV) (p-value = 0.079) and tenofovir (TDF), lamivudine (3TC) and efavirenz (EFV) (p-value = 0.075) were marginally significant. There were no statistically significant with factors and patients' body weight from 50 to 70 weights.

Table 5. Multinomial odd ratios (OR) of the association for patients' body weight at 12 months

Factors	Weight at 12 months of ART			
	Less than 50 weight		Between 50 to 70 weights	
	OR (95% CI)	P-values	OR (95% CI)	P-values
Age group (ref. >50)				
<25	1.89 (0.46, 7.74)	0.38	1.47 (0.53, 4.09)	0.45
25-49	0.81 (0.23, 2.86)	0.75	1.72 (0.74, 4.04)	0.20
Sex (ref. female)				
Male	0.39 (0.20, 0.76)	0.01	0.97 (0.66, 1.42)	0.88
Facility (OC)				

KHC	0.88 (0.47, 1.63)	0.69	1.18 (0.80, 1.73)	0.40
Hepatitis B (ref. negative)				
Positive	1.04 (0.42, 2.54)	0.94	0.74 (0.42, 1.31)	0.30
ART regimens (Others)				
TDF/FTC/EFV	0.24 (0.05, 1.18)	0.07	0.66 (0.18, 2.46)	0.54
TDF/3TC/EFV	0.24 (0.05, 1.13)	0.07	0.68 (0.19, 2.49)	0.56
TDF/3TC/NVP	0.21 (0.04, 1.03)	0.05	0.56 (0.15, 2.09)	0.39

The reference category: more than 70 weights.

Discussion

In this retrospective cohort study, the aim was to investigate the outcomes and determinant of ART treatment adherence. The two health-related outcomes considered after ART initiation were viral suppression and weight gain. Specifically, we compared the viral load suppression and weight both at 6 months and 12 months by ART treatment adherence and to explore if there is an association between health-related outcomes and ART adherence, using a clinical cohort in Windhoek, Namibia. Patient adherence to ART treatment is a crucial component in the successful outcome of HIV treatment. The consequence of non-adherence is not only early death due to inconsistent uptake of treatment, but also enables development of drug resistance (Heestermans et al., 2016; Olowookere et al., 2016; Reda & Biadgilign, 2012).

We found that a good proportion of patients were found to significantly adhere to ART treatment (69.1%), once they get started on treatment. This finding is similar to that found by Peltzer et al, (2010) where 70.8% HIV patients in KwaZulu-Natal, South Africa, adherent to ART treatment. In some societies this can be even much higher, for example, in Ethiopia (Ketema and Weret, 2015). Be as it may, studies in same countries have also reported low adherence (Boyles et al. 2011; Markos et al., 2009; Ncaca et al., 2011). The difference in adherence has been attributed to a number of factors including the methodology (Ketema and Weret, 2015), and socio-economic and demographic factors (Heestermans et al., 2016), as well as belief in alternative medicines (Ketema and Weret, 2015; Ncaca et al., 2011). The need therefore to study determinants of treatment adherence to ART is necessary in various settings.

In this study, we considered age, sex marital status, WHO clinical stage, and treatment regimen as possible determinants of treatment adherence. As a clinical retrospective cohort study, our study was limited in the number of factors that were studied. We found that being married, and being of age between 25 to 49 years old, and being at WHO clinical stage I (at the start of the ART) had a positive inclination towards adherence to treatment. This finding is in line with other studies on the determinants of ART adherence (Heestermans et al., 2016; Olowookere et al., 2016; Reda & Biadgilign, 2012). Our finding was inconsistent with the study conducted by Noens, et al. (2009) where 202 patients were recruited from 34 centers in Belgium, of whom 169 were evaluable and the majority of patients were male (55.0%) and were considered to be non-adherent.

A number of explanations are possible. Being married, the spouse or partner may have provided an immediate treatment supporter, which is a known fact in HIV/AIDS treatment (Nachenga et al, 2006). In some cases treatment supporter can be nominated from communities (Nachenga et al, 2010), or use mobile messages for daily reminders (Hirsch-Moverman et al., 2017). Be as it may, marriage partners have been found to provide much needed confidante, while eliminating a sense of stigma and discrimination for HIV patients (Duwell et al, 2013; Johnson et al, 2012), thus enhancing treatment adherence. With regards to age, there are mixed facts that explain how it improves adherence. Others have argued that with right messaging at treatment counselling, patients of young age have all the reasons to live for. They are encouraged to adhere to treatment, leading to viral load suppression, and enhanced positive dignified and productive life in later years (Mathes et al, 2014). Nevertheless, most studies found that higher age is associated with higher adherence (Heestermans et al., 2016; Olowookere et al., 2016; Reda & Biadgilign, 2012; Markos et al., 2009; Ncaca et al., 2011). With regards to clinica stages, being at stage I provides improved prognosis much earlier after initiating treatment, and therefore reduces loss-to-follow up among patients (Rougemont et al, 2009), moreover, those at stage I are less likely to die (Fonsah et al., 2017).

Excellent adherence to antiretroviral treatment (ART) is vital for treatment success (Nachega 2010). Two outcomes: viral load suppression and weight gain are well known outcomes of patients retained on treatment. Our study confirms that HIV patients reach viral load suppression and achieve body weight both at 6 months and 12 months when ART adherence was more than 95%. Anything lower does not give better outcomes. The study further found that viral suppression was associated with WHO clinical stage. Suprisingly, the HIV patients who at clinical stage I (OR: 0.30, 95% CI: 0.12-0.75, p-value = 0.010) and stage-II (OR 0.26, 95% CI 0.09-0.75, p-value = 0.010) were less likely to be associated with viral load suppression at 6 months, which was a reverse under determinants of treatment adherence. Patients who were at clinical stage-I and those treated with a combination ART regimen containing tenofovir (TDF) or emtricitabine (FTC) neither efavirenz (EFV) were less likely to be associated with viral load suppression at 12 months. Be as it may, our findings were consistent with those of other studies in demonstrating the importance of the initial ART regimen in the rate of achieving viral load suppression at 12 months (Noens et al, 2009; Heestermans et al., 2016; Olowookere et al., 2016).

Regarding patients' body weight at 6 months, significant determinants included being male and ART regimens among patients with body weight of less than 50 weights. The ART regimens are the combination of pills containing tenofovir (TDF) or emtricitabine (FTC) neither efavirenz (EFV), tenofovir (TDF) or lamivudine (3TC) neither efavirenz (EFV) and tenofovir (TDF) or lamivudine (3TC) neither nevirapine (NVP). On the other hand, those of body weight from 50 to 70 weights, there were no comparable determinants, when compared to those with patients of weight of more than 70 kgs. A similar pattern was observed for body weight at 12 months, such that being male and taking nevirapine-based regimens and efavirenz-based regimens associated with weight gain among patients of 50 kg or less.

Conclusion

It is evident that treatment adherence leads to better outcomes for HIV patients. Both demographic and clinical factors, though of limited scope, were associated with ART adherence and outcomes. Future research should consider evaluating the effect of adherence to an extended coverage of clinics, and allow collecting more detailed factors that are associated with treatment adherence. Such design targeted interventions may assist to optimize treatment adherence and health-related outcomes.

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