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Prevalence and correlates of first line Antiretroviral therapy change among adult HIV patients attending HIV care and treatment services in north western rural part of Tanzania: a cross sectional study

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Abstract

Background

HIV/AIDS is an ongoing health problem causing still high morbidity and mortality. ART have provided significant clinical benefits leading into reduced mortality and morbidity which requires tolerable, affordable and virologically potent regimens for its durability. Frequent need for change of ART regimes is a challenging problem especially in resource limited settings including Tanzania where there are few options to switch into. This study was designed to determine the frequency, reasons and predictors of ART change in rural Tanzania.

Materials and Methods

A cross sectional study was done involving adult HIV positive patients who were initiated on ART between 2005 and 2014. The patients were enrolled serially through routine HIV care and treatment services in eastern rural part of Lake Zone. Information of research interest including demographic data, on diagnosis WHO clinical stage, baseline CD4 counts, year and criterion of ART initiation, initial ART regimen, ART change status, reason for ART regimen change, time on initial ART and enrollment CD4 counts were collected and analyzed using stata version 12.

Results

A total of 670 patients were enrolled in this study where 220(32.94%) were found to have changed their ART regimen with a first line regimen of 27.5 [IQR=14-38] months. ART toxicity was the most common reason of ART change which 106 (48.18 %) and the odds of having ART change were strongly predicted by age>40, being divorced(OR=2.4 ,p=0.0012), baseline CD4 counts <200 cells/µl (OR=3.9, p<0.001), being initiated on ART due to low CD4<200 cells/µl(OR=2.0, p<0.001) or being initiated on ART with CD4< 350 cells/µl and WHO clinical stage 3(OR=2.2, p<0.001) and d4T based regimen (OR=138, p<0.001)

Conclusions

ART change is a very frequent problem in rural Tanzania, which is strongly predicted by diagnosis of HIV in older patients, Advanced HIV parameters and d4T based regimens. Universal screening programs to diagnose HIV in earlier ages and in less advanced HIV parameters and subsequent early initiation of less toxic ART regimens could significantly contribute to the reduction of this problem in our setting where we have limited potent options to go for.

Key words: HIV/AIDS, adult HIV patients, initial ART regimen change, rural Tanzania

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Introduction

HIV/AIDS is still an ongoing global health problem causing significantly high morbidity and mortality especially in resource limited countries. The virus is notable for its effect on reduction in number and quality of functional CD4 T- cells, causing high morbidity and mortality from opportunistic infections (OIs) [1]. Since its discovery in 1981, about 34 million people have died of HIV/AIDS related causes [2]. The mainstay of HIV management remains to be an effective highly active anti retroviral therapy (HAART). HAART reverses the consequence of HIV/AIDS through continued suppression of viral replication hence reducing the viral load; allowing CD4/immune recovery [3]. These effects are clinically vital that, CD4 recovery restores the body's capacity to fight against OI reducing morbidity and mortality of people living with HIV/AIDS (PLHA) [4, 5] whereas the reduction of plasma HIV viral load reduces HIV transmission rate [6] potentially reducing the number of new HIV cases.

Indeed the introduction of ART has provided remarkable clinical benefits. With the use of ART, HIV has been converted into a chronic manageable disease [7, 8] as a result of an overall significant reduction of HIV/AIDS related morbidity and mortality [9, 10].The clinical benefits of ART are mediated through a durable suppression of viral replication. Because ART doesn't eradicate the virus, these therapeutic effects require an un-interrupted lifelong treatment [11]. In this background there has been a rapid scaling up of access to HIV care and treatment including sub Saharan Africa region where more than 70% of the world's HIV cases are located [12]. .
Even with these successes a frequent need of ART regime change is an important challenge that can significantly affect the durability of the available ART combinations. This is particularly important in resource limited settings like Tanzania where there are few ART alternatives which are cheap and less complex that we can go for[13]. This may lead into delayed change and in effective virological and clinical response. In our setting the information on the magnitude of this problem is scarce. This study was therefore designed to determine the frequency, reasons and

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predictors of first line ART change among adult HIV positive patients attending care and treatment services in rural Tanzania.

Materials and methods

Study design and settings

This was a cross sectional hospital based study involving HIV patients on ART who were attending a routine care and treatment services at Tarime district hospital. Tarime is one of the seven Mara region's administrative districts located in north-eastern part of Lake Zone in Tanzania. Tarime district hospital serves a catchment area of more than 35000 people running both inpatient and outpatient services with a bed capacity of about 200. HIV/AIDS care and treatment services are routinely done as part of outpatient services currently serving about more than 5000 HIV positive patients. This study was conducted between June and December 2015 as part of elective field work involving all HIV positive patients who were initiated on ART between 2005 and 2014.

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Sample size, Patients' enrollment and data collection

A minimum sample size of 384 was estimated using the cross sectional study's formula by Leslie Kish assuming 50% of HIV patients on ART had their regimen change due to various reasons with a prevalence range of 18-78% from prior studies [14, 15]. Patients who presented to Tarime district hospital CTC were invited to participate in the study and those who started on ART between the specified periods were requested to participate in this study. All patients young than 18 years were excluded from the study, and after informed consent the patients records were reviewed and the information of research interest were collected in a special tool including demographic (Age, sex, marital status, level of education and occupation), WHO clinical stage, the initial ART regimen, an ART change status and reason of change as recorded in patients files, time on the first ART regimen, baseline and on enrolment CD4counts.

Definition of variables and data management

In this study first line ART was defined as a combination of 2 nucleoside reverse transcriptase inhibitors with one non nucleoside reverse transcriptase inhibitor or a protease inhibitor with or without a pharmacological booster. All patients were treated with combined ARTs standard

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doses of AZT (300mg BID), d4T (40mg or 30mg BID for weight>60Kg or <60Kg respectively), TDF (300mg OD) 3TC (300mg OD), EFV (600 OD), NVP (200mg BID), and LPV/r (200/50mg BID). Treatment failure in this study was defined clinically a development of a new stage 3 or 4 AIDS defining condition while on ART, or immunologically as having a fall of CD4 count by 50% form peak value ever reached, or a fall of CD4 count to baseline CD4 level or a persistently low CD4 count less than 100 cells/µl after a year of ART [16]. Patients with toxicity were those who developed clinically important side effect on the course of their ART requiring a change or modification of their regimen including severe anemia, change of fat distribution, skin rashes among others [15, 17]. Data were computerized using Epi data version 3.1 and STATA version 11 (Stata Corp LP, college station, TX) was used for data analysis. Continuous variables were expressed as means with interquartile range (IQR) while categorical variables were expressed as proportions with percentages. The proportion of patients who had their ART regimen change was calculated and the reasons for change were recorded. The effect of different risk factors on the odds of having ART change was investigated. The Odds ratio with 95% Confidence Interval (CI) was calculated using univariate analysis followed by multivariate analysis model to assess the extent of association of different variables to the outcome of interest. In all our analysis factors were said to be statistically significant when the p value was less than 0.05.

Ethical clearance

The permission to conduct and publish the findings from this study was sought from the catholic university of health and allied sciences/ Bugando medical center joint ethical committee. Patients provided written consent for the study and their identifiers including names and registration

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Results

The basic socio-demographic, clinical and laboratory characteristics of the study participants

During the study period a total of 670 patients were enrolled with a median age of 39 [IQR=32-44], most of them 413(61.64) being females with a female to male ratio of 1.6:1. Most of the study participants 325(48.51%) were married, and more than 46% were primary school drop outs. The study participants were mainly peasants 325 (48.06 %) and majority of them 401(59.85%) were in WHO clinical stages 3 and 4 at the time of diagnosis with a median baseline CD4 count of 242[IQR=131-329] cells/µl. The most common first line ART regimen 294(43.88%), was TDF+3TC+EFV with a mean time on first line regimen of 27.5[IQR=14-38] months as summarized in **table 1.**

The prevalence and risk factors of first line ART change among adult HIV positive patients attending a rural HIV care and treatment services in Tanzania

In this study 220 (32.84%) of the study participants had changed their first line ART regimens where 106 (48.18 %) of these changes were due to side effects, while 70(31.82%) and 44(20.0%) were due to treatment failure and TB treatment initiation respectively (table 1). On univariate analysis the frequency of change of ART regimen was strongly associated with the age of more than 40 years(OR=1.8, p<0.001) which showed no significant association on multivariate analysis, while on both univariate and multivariate analysis the frequency of ART change was strongly predicted by a marital status of being divorced(OR=2.4 ,p=0.0012), low baseline CD4 counts <200 cells/µl (OR=3.9, p<0.001), being initiated on ART due to low CD4<200 cells/µl(OR=2.0, p<0.001) or those who were initiated on ART due to CD4 counts of less than 350 cells/µl and WHO clinical 3(OR=2.2, p<0.001) and being on the first line d4T based regimen (OR=138, p<0.001) as summarized in table 2. On a sub analysis patients who changed ART regimen due to toxicity were more likely to be those older than 40 years (OR=2.3, p<0.001), the divorced patients (OR=2.3,p<0.002), those who had a baseline CD4 counts <200 cells/µl(OR=2.1, p<0.001), those who were initiated on ART due to low CD4 counts(OR=3.4,

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p=0.001) or CD4 counts <350 and WHO clinical stage 3(OR=1.9, p=0.007), and those who were on the initial d4T based ART regimen (OR=18, p<0.001). On the other hand patients whose regimens were changed due to treatment failure were likely to be those who were married(OR=1.6,p=0,044), with primary education level (OR=1.7, p=0.003), baseline CD4 counts <200cells/µl (OR=2.3, p=0.001), those who were initiated on ART due to low CD4 counts (OR=1.2, p=0.0023) and those who were on d4T based regimen (OR=5.8, p<0.001). While patients who changed ART regimens due TB were mostly those who were married (OR=1.9, p<0.041), with low baseline CD4<200cells/µl (OR=2.5, p=0.004) or being initiate on ART in WHO clinical stage 4 (OR=1.3, p=0.007) and those who were on d4T based regimen (OR=8.3, p=0.001) (Table 3). The distribution of all other factors was not statistically significant

Discussion

The objective of this study was to determine the frequency, reasons and risk factor of initial ART regimen change among adult HIV positive patients attending care and treatment services in north eastern rural Tanzania. In this study a total of 220 (32.94%) patients changed their ART regimen with ART side effects being the most common cause of ART change followed by ART treatment failure and occurrence of TB. In this study, first line ART regimen change was predicted by parameters of advanced HIV at the time of diagnosis and treatment initiation. These findings are in agreement with findings from previous studies with ART change rate ranges of 18-78% in most settings. For example Inzaule et al. in 2014 reported a rate of 18.7% in western Kenya [14]. Another study in china by Sun and colleagues reported a rate of 25.8% [18] while a rate of 27.3% was reported earlier in 1990 by Van Roon et al in Netherlands [19]. On the other hand much higher rates of ART change have been reported previous in several other studies. For instance a rate of 36.2% was reported in 2000 from an Italian study by Monforte et al. [20] whereas in another study from Thailand 41% of patients on first line ART changed their regimen [21]. While 62% of ART change was reported in Kenyan study in 2010 [22], an even high rate of 78.4% was reported previously in 2007 in Western Kenya [15]. These higher rates of first line ART change could partly be explained by the differences in study methods. For instance in

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Kenyan a longitudinal study collected data from patients which are more likely to pick more ART related events than retrospectively conducted studies like ours.

In the index study the commonest cause of ART change was drug toxicity. Of the 220 patients who had ART change 106 (48.18%) were due to toxicity while 70 (31.82%) and 44 (20%) were due to treatment failure and Tb respectively. Studies from elsewhere have reported similar observations. For example in studies from Kenya toxicity being the most common reason of ART change was reported in 46- 66% of patients who had their ART regime changed [14, 22]. In another study form Thailand ART toxicity was reported in more than 73% of ART changes whereas treatment failure and TB was reported in 63 (16.7%) and 16 (4.2%) of the study participants respectively [21]. In a Chinese study up to 92.4% of patients who had ART change were due to drug toxicity while treatment failure was reported to contribute only 5.1% of the ART changes [18].

On clinical grounds ART drug related adverse effects are documented as one of the important causes of non adherence to ART medications and this can negatively affect the ART outcomes [23, 24], and this may take different forms of presentations clinically depending on the combination ART that the patient is on though they have been reported with essentially all AR combinations. Lipodystrophy neuropathy, CNS adverse effects, skin rashes and anemia are commonly reported in several studies settings [18, 25-27]. In the index study Lipodystrophy and anemia were the commonest form of ART toxicity reported in 55 (51.80%) and 18 (16.98%) of those with recorded toxicities (table 3b) which were related to d4T containing regimen 05/55(90.91%) and AZT containing regimen 12/18(66.6%) respectively.

On comparing the distribution of variables between those with ART change and those without ART change several factors were independently associated with ART change including older age >40 years on univariate analysis, being divorced, baseline CD4 count <200cells/µl, and being started on ART due to low CD4 and being on d4T based regimen. Most of the findings from the index study are in agreement with findings from several other studies [14, 18, 28]. Most prior studies have suggested that patients with older age than 40 years have reduced renal functions

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and are liable to most drug toxic effect including D4T and AZT [29, 30]. This is also supported by our study where upon testing for interaction, patients older than 40 years were likely to have toxicity (OR=2.3, P<0.001) as a cause of their ART drug change especially from D4T (OR=1.9, P< 0.001). Advanced HIV parameters (CD4 counts <200 cells/µl and WHO clinical stage 3&4 have been shown to have a higher risk of adverse ART reactions [22] which is also supported by our findings (Table 3). In the current study these patients are additionally at a higher risk of treatment failure and development of opportunistic infection like TB with a subsequent change of ART regimen. It has been in from studies that this sub group of patients has poor immune recovery on receipt of ART [31-33]. For instance it was demonstrated from a study by Hunt and colleagues that less than 50% of patients starting on ART at CD4 levels lower than 200 cells/µl reach a threshold of 350 cells/µl even after 4 years of potent ART [34], with increased risk of opportunistic infections among other consequences.

Stavudine has long been known for its mitochondria toxic effect presenting with neuropathy and Lipodystrophy [35]. These complications are likely to affect compliance to ART medications negatively [23, 24] which may lead into treatment failure and clinical deterioration. This is in agreement with our study findings that patients who were on d4T based regimen were more likely to have a switch of their regimen due to treatment failure (OR=5.8, p<0.001) and TB (OR=8.3, p<0.001) in addition to development of ART related toxicities (OR=18, p<0.001). In this study the TB could have developed as a part of treatment failure or else the switch could have been because of the NVP component of the stavudine combined ART. In this way though stavudine used to be the cheapest, highly efficient virologically and readily available ART [36, 37]; however its mitochondrial mediated side effects are very limiting as reported also in a numbers of other studies [37, 38] supporting the phasing out of its use [39, 40] as compared to Tenofovir [41] based regimen.

This study had a number of limitations. This was a cross sectional study and a single center hospital based one therefore the results from this study may not be generalizable. With lack of viral load facilities the treatment failure was not confirmed virologically this could have affected the number of ART switches since immune-clinical criteria are shown to be less sensitive [42,

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43]. The findings from this study are clinically very important especially in resource limited settings like Tanzania where there are limited options for new ART combination. The alternative ART regimens have been shown to be more expensive and complex in addition to a need for closer laboratory monitoring and frequent Clinic visits. In this context patients are likely to be on a non favorable regimen much longer which may adversely affect the overall outcome of ART. In the background of these facts clinicians should take greater efforts to diagnose HIV early enough and in younger ages to improve the durability of the affordable and less complex ART regimen where universal screening for HIV may be a better strategy.

Conflict of interest

Authors declare to have had no conflict of interest. All authors read and approved the final manuscript draft.

Authors' contribution

DWG: conceived the idea, designed the study, analyzed the data, searched the literature, drafted the manuscript; **AGS:** assisted in designing the study, acquired the data, assisted in interpreting the data and critically reviewed the manuscript for its intellectual content; **BCTM:** assisted data analysis and interpretation, literature search and critically reviewed the manuscript for its intellectual content; **SBK:** assisted data analysis, literature search and critically reviewed the manuscript for its intellectual content; **ERS:** assisted data interpretation, literature search and critically reviewed the manuscript for its intellectual content.

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Tables of Results

Tables 1: The socio-demographic, clinical and laboratory characteristics 670 study participants

Variable	Frequency	Median (IQR) or Percent
Age (Years)	670	39 [32-44]
Sex		
Male	257	38.36
Female	413	61.64
Marital Status		
Divorce	087	12.99
Married	325	48.51
Single	067	10.00
Widow	191	28.51
Level Of Education		
Illiterate	60	08.96.
Primary Education	311	46.42
Secondary Education	181	27.01
College Education	118	17.61
Occupation		
Peasant	325	48.51
Business	222	33.13
Formal Employee	84	12.54
Driver	24	03.58
Students	15	02.24
Baseline WHO Stage		
3&4	401	59.85
1&2	269	40.15
Baseline CD4 Count	670	242[131-329]
Enrolment CD4 Counts	670	407[256-548]
The first line cART		
AZT+3TC+ EFV	104	15.52
AZT+ 3TC+NVP	114	17.01
D4T+3TC+NVP	158	23.58
TDF+3TC+EFV	294	43.88
Reason For ART Change	220	
ART Change		
Yes	220	32.84
No	450	67.16
Durability Of First Line (Mo)	670	27.5[14-38]
Reason For ART Change	220	
Toxicity	106	48.18
Treatment Failure	070	31.82
TB Infection	044	20.00

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Abbreviation: CD4: Cluster of Differentiation 4; IQR: interquartile range; WHO: World health Organization

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Table 2: The univariate and multivariate analysis for factors associated with cART change (n=670)

Factor		cART Regime Change		Un-adjusted		Adjusted	
		No	Yes	OR (95%CI)	p	OR (95%CI)	p
Sex							
	Male	181 (40.22)	076 (34.55)				
	Female	269 (59.78)	144 (65.45)	0.8 (0.56- 1.1)	0.156		
Age group							
	>40 years	155 (34.44)	108 (49.09)				
	<40 years	295 (65.56)	112 (50.91)	1.8(1.3- 2.5)	0.000*	1.2(0.9-1.6)	0.220
Marital Status							
	Divorce	045 (10.00)	042 (19.09)	2.1(1.3-3.4)	0.001*	2.4(1.2-4.8)	0.012*
	Married	211 (46.89)	114 (51.82)	1.3(0.9-1.7)	0.173		
	Single	046 (10.22)	021 (09.55)	1.0 (0.6-1.7)	0.929		
	Widow	148 (32.89)	043 (19.55)	0.5 (0.3-0.7)	0.000		
Level Of Education							
	Illiterate	041 (09.11)	019 (08.64)	0.9(0.5-1.6)	0.768		
	Primary Education	203 (45.11)	108 (49.09)	1.2 (0.8-1.6)	0.390		
	Second Education	128 (28.44)	053 (24.09)	0.8 (0.6-1.2)	0.234		
	College Education	078 (17.33)	040 (18.18)	1.0 (0.6-1.6)	0.843		
Occupation							
	Peasant	220 (48.89)	105 (47.73)	1.0(0.7-1.3)	0.778		
	Business	144 (32.00)	078 (35.45)	1.1(0.8-1.6)	0.438		
	Formal Employee	054 (12.00)	030 (13.64)	1.2(0.7-1.9)	0.446		
	Driver	020 (04.44)	004 (01.82)	0.4(0.1-1.2)	0.096		
	Students	012 (02.67)	003 (01.36)	0.5(0.4-1.8)	0.293		
Baseline WHO Stage							
	3&4	263 (58.44)	138 (62.73)				
	1&2	187 (41.56)	082 (37.27)	1.2(0.9-1.7)	0.288		
Baseline CD4 Count							
	<200	133 (29.56)	121 (55.00)	2.9(2.1-4.1)	0.000*	3.9(2.3-6.6)	0.000*
	200-350	188 (41.78)	085 (38.64)	0.9(0.6-1.2)	0.437		
	>350	129 (28.66)	014 (06.36)	0.2(0.1-0.3)	0.000		
Reason for ART							
	Low bCD4	158 (35.11)	123 (55.91)	2.3(1.7-3.3)	0.000*	2.0(1.2-3.4)	0.005
	CD4/WHO criterion	128 (28.44)	010 (04.55)	0.3(0.2-0.5)	0.000		
	WHOs criterion	164 (36.44)	087 (39.55)	1.0(0.9-1.2)	0.436		
Initial cART regimen							
	AZT backbone	152 (33.78)	066 (30.00)	0.8(0.6-1.2)	0.327		
	d4T backbone	008 (01.78)	150 (68.18)	118(55-251)	0.000*	138(62-305)	0.000*

	TDF backbone	290 (64.44)	004 (01.82)	0.01(0-0.03)	0.000		

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Table 3: Factors associated with reasons of change or modification of ART regime among 220 patients

Factor	Toxicity (n=106)			Treatment failure (n=70)			Tuberculosis (n=44)		
	N %	**OR (95%CI)**	**P value**	**N%**	**OR (95%CI)**	**P value**	**N%**	**OR (95%CI)**	**P value**
Sex									
male	32(30.19)			23 (32.86)			21(47.7)		
female	74(69.81)	0.7(0.4-1.0)	0.061	47 (67.14)	0.8(0.5-1.3)	0.318	23(52.3)	1.5(0.8-2.8)	0.189
Age group									
>40years	60(56.60)			27(38.57)			21(47.7)		
<40yreas	46(43.40)	2.3(1.5-3.5)	0.000*	43(61.43)	1.0(0.6-1.6)	0.902	23(52.3)	1.4(0.8-2.7)	0.236
Marital Status									
Divorced	24(22.64)	2.3(1.3-3.9)	0.002*	11(15.7)	1.3(0.6-2.6)	0.474	07(15.9)	1.3(0.6-3.0)	0.552
Married	45(42.45)	0.7(0.5-1.1)	0.175	41(58.6)	1.6(1.0-2,7)	0.044*	28(63.6)	1.9(1.0-3.7)	0.041*
Single	13(12.26)	1.2(0.7-2.3)	0.490	07(10.0)	1.3(0.6-2.6)	0.479	01(02.3)	0.2(0.0-1.5)	0.114
Widow	24(22.64)	0.7(0.4-1.1)	0.137	11(15.7)	0.4(0.2-0.8)	0.014	08(18.2)	0.5(0.2-1.1)	0.117
Educational level									
Illiterate	10(09.52)	1.0(0.5-2.1)	0.898	03(04.29)	0.4(0.1-1.4)	0.151	06(13.95)	1.6(0.7-4.0)	0.284
Primary	46(43.81)	0.9(0.6-1.3)	0.518	41(58.57)	1.7(1.0-2.9)	0.031*	20(46.51)	1.0(0.5-1.8)	0.911
Secondary	33(31.43)	1.3(0.8-2.0)	0.299	13(18.57)	0.6(0.3-1.1)	0.096	07(16.28)	0.5(0.2-1.1)	0.092
College	16(15.24)	0.8(0.5-1.5)	0.511	13(18.57)	1.1(0.6-2.1)	0.769	10(23.26)	1.4(0.7-3.0)	0.329
Occupation									
Peasant	53(50.3)	1.1(0.7-1.6)	0.738	38(54.3)	1.3(0.8-2.1)	0.308	14(31.8)	0.5(0.2-0.9)	0.025
Business	37(35.2)	1.1(0.7-1.7)	0.647	20(28.6)	0.8(-0.5-1.4)	0.407	19(43.2)	1.8(1.0-3.3)	0.072
Formal Employ	12(11.4)	0.9(0.4-1.6)	0.645	16(17.1)	1.5(0.8-2.9)	0.239	07(15.9)	1.3(0.5-3.0)	0.508
Driver	01(01.0)	0.2(0.0-1.7)	0.145	00(0.00)	-	-	03(06.8)	2.1(0.6-7.3)	0.242
Students	02(01.9)	0.8(0.2-3.7)	0.790	00(0.00)	-	-	01(02.3)	1.0(0.1-7.9)	0.987
WHO Stage									
3&4	76(71.70)			41(58.57)			21(47.73)		
1&2	30(28.30)	1.9(1.2-2.9)	0.007*	29(41.43)	1.190.6-2.1)	0.769	23(52.27)	1.4(0.7-3.0)	0.329
Baseline CD4									

	<200	56(52.83)	2.1(1.4-3.1)	0.001*	39(55.71)	2.3(1.4-3.7)	0.001*	26(59.09)	2.5(1.4-4.7)	0.004*
	200-350	41(38.68)	0.9(0.6-1.4)	0.637	29(41.43)	1.0(0.6-1.7)	0.902	15(34.09)	0.7(0.4-1.4)	0354
	>350	09(08.49)	0.3(0.1-0.6)	0.001	02(2.86)	0.1(0.0-.4)	0.001	03(06.82)	0.3(0.1-08)	0.024
Reason for ART										
	Low CD4	71(66.98)	3.4(2.2-5.3)	0.001*	35(50.00)	1.4(0.9-2.4)	0.151	17(38.64)	0.9(0.5-1.6)	0.646
	CD4/WHO	08(07.55)	0 .5(0.4-0.8)	0.001	00(00.00)	-	-	02 (04.55)	0.4(0.2-0.8)	0.016
	WHO st4	27(25.47)	0.8(0.6-0.9)	0.006	04(50.00)	1.2(1.0-1.4)	0.023*	25(56.82)	1.3(1.1-1.6)	0.007*
inART regimen										
	AZT backbone	26(24.53)	0.6(0.4-1.0)	0.057	26(37.14)	1.3(0.7-2.1)	0.386	14(31.82)	1.0(0.5-1.9)	0.916
	d4T backbone	79(74.53)	18(10-30)	0.000*	41(58.57)	5.8(3.4-9.8)	0.000*	30(68.18)	8.3(4.2-16.2)	0.000*
	TDF backbone	01(00.94)	-	-	03(04.29)	-	-	0.0(00.00)	-	-

Abbreviation: **ABC:** abacavir; **AZT:** Zidovudine; **ART**: antiretroviral therapy; **CI:** confidence interval; **CD4:** cluster of differentiation 4; **d4T:** stavudine; **inART**: initial ART; **IQR**: interquartile range; **N:** number or frequency; **OR:** odds ratio; **st:** stage; **WHO**: world health organization;

Table 3b: Forms of toxicity stratified by combined ART regimen among 106 patients with ART change

Form of toxicity	AZT+ 3TC+ NVP	AZT+ 3TC+ EFV	D4T+3TC+NVP	TDF+3TC+ EFV	Total
Lipodystrophy	2 (03.64%),	2 (03.64%)	50(90.91%)	01(1.82%)	55 (51.80%)
Anemia	9 (50.00%)	3 (16.67%)	06(33.30%)	00(0.00%)	18 (16.98%)
Neuropathy	2 (11.76%)	4 (23.53%)	11(64.71%)	00(0.00%)	17 (16.04%)
Skin rashes	3 (18.75%)	1 (06.25%)	12(75.00%)	00(0.00%)	16 (15.09%)

AZT: Zidovudine; **3TC:** Lamivudine; **D4T:** stavudine; **EFV**: Efavirenz; **NVP:** Nevirapine; **TDF:** Tenofovir