Outcomes and Rates of CD4 cells decline among HIV-positive patients in Pre-Antiretroviral Therapy Care

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ABSTRACT

Background: The CD4 cells count is a marker of HIV disease progression and a criterion for initiation of antiretroviral therapy (ART).

Objectives: This study evaluated the outcomes and CD4 cells decline rates among HIV-positive patients enrolled into pre-ART care in Nigeria.

Methods: In a five-year retrospective cohort assessment, 1,098 patients were randomly selected from 1766 HIV positive patients who were ineligible to start ART and enrolled into pre-ART care during 1st March to 31st December 2007 in two health facilities. Routine clinical and immunologic data were extracted from patients' hospital records starting from pre-ART care enrolment and ending April 30, 2012. Paired sample *t-test and* Chi-square were used for inferential statistics; and P<0.05 indicated statistical significance.

Results: The patients' mean age was 33.1 (95%CI, 32.6–33.6) years old; and 65.1% were females. Patients' follow-up in pre-ART care was 512.6 person-years. During the 5-year observation period, there was a significant decline in CD4 cells count (cells/mm^3) at months 3, 6, 12, 18, 30 and 42 (P<0.05). The mean CD4 cells count decline rate was 2.5 (95%CI, 2.1–2.9)cells/mm^3 per annum. Pre-ART outcomes included 56.1% started ART, 39.7% loss to follow up, 2.6% transferred-out, 0.9% active in pre-ART care and 0.5% were dead at the end of observation period. The outcomes were associated with baseline WHO clinical stage and CD4 cells count (P<0.05).

Conclusion: Majority of patients started ART. There was a significant decline in CD4 cells count of pre-ART patients; and the decline rate was very low compared to previous reports.

Key words: Pre-ART, immunologic, HIV care, outcomes, patients, Nigeria

INTRODUCTION

The number of people living with Human Immunodeficiency Virus (HIV) globally has continued to grow from 29.5 million in 2002 to 34.0 million in 2010.[1] The prevalence of HIV in Nigeria is 4.1%; and it is estimated that 3.15 million people are living with HIV. Out of this population, about 1.56 million require antiretroviral drugs but only 415,000 of them are receiving it.[2] This implies that a greater proportion of these people (about 1.59 million) in Nigeria are expected to be on pre-antiretroviral therapy (pre-ART) care until antiretroviral therapy (ART) eligibility. Pre-ART care as stipulated in the Nigerian national HIV treatment and care guideline included periodic ongoing counselling, health education and periodic CD4+ estimation.[3]

Following HIV seroconversion, the immune system cells (including CD4 cells) is slowly destroyed by HIV. If the HIV-infected patient is not initiated on ART, the immune system gradually loses the ability to fight off infections and the patient may develop opportunistic infections that determine the diagnosis of acquired

immune deficiency syndrome (AIDS).[4] The patients' CD4 cells count is a marker of HIV disease progression and a criterion for initiation of ART.[4-7] The changes in CD4 cells counts and viral load are also used assess the response to ART.[7] The rate of CD4 cell decline in pre-ART patients is highly variable over time. However, this rate is a poor predictor of the risk of AIDS or death in pre-ART patients as there is no association between pre-ART CD4 slope and survival.[4] There is no evidence that knowledge of pre-ART CD4 cell slope improves the prediction of the risk of a new AIDS event or death.[4] In Singapore, the overall average rate of CD4+ T-cell decline in pre-ART patients without regard to HIV-1 subtype was 56 cells/ mm^3 per year.[8] In North America, Australia and Europe, studies have reported higher rates of CD4 cells count decline between - 33 and - 77 cells/ mm^3 per year[4, 9, 10]; compared to the estimated decline rates ranging from - 21.5 to - 47.1 cells/ mm^3 per year reported in sub–Saharan Africa.[11-14] Wolbers *et al* (2010) also reported that the proportion of patients with a CD4 cell decline >100 cells/ mm^3 per year varied from 13% to 54%.[4] Some treatment guidelines recommend ART initiation given a rapid CD4 cell count decline of >50 to 100 cells/ mm^3 per year.[15-16] There are no studies reporting outcomes and CD4 cells decline rates in pre-ART patients in Nigeria to our knowledge. This study evaluated the pre-ART care outcomes and CD4 cells count decline rates among patients testing positive for HIV who are ineligible to start ART in Nigeria.

METHODS

Study Design

The study employed a retrospective cohort design. Patients testing positive for HIV who were ineligible to start antiretroviral therapy (ART) and enrolled into pre-ART care during 1st March to 31st December 2007 were assessed using routine clinical, immunologic and outcome data from the patients' hospital records. Pre-ART care was based on the Nigerian national ART guideline.[3]

Setting

This study was carried out in two secondary public health facilities (General Hospital Minna, Niger State and Maitama District Hospital, Abuja FCT) in North-Central Nigeria. The hospitals offer comprehensive HIV care services including ART (at no cost to the clients) with funding support from President's Emergency Plan for AIDS Relief (PEPFAR) through United States Agency for International Development (USAID). Maitama District Hospital Abuja and General Hospital Minna started providing the PEPFAR supported comprehensive HIV care services in March 2007 and May 2007 respectively. Patients testing positive for HIV and were not eligible to commence ART were enrolled into a Pre-ART register for HIV care and follow-up; and only those who meet the eligibility criteria for starting ART based on the guideline for HIV treatment and Care in Nigeria[3] were commenced on treatment. Pre-ART care as stipulated in this guideline included periodic ongoing counselling, health education and periodic CD4+ estimation.[3]

Study population and sample

The study population included a total of 1766 HIV positive patients who were ineligible to start ART and enrolled into pre-ART care register. This included 856 patients enrolled between May 1, 2007 to December 31, 2007 in General Hospital Minna; and 910 patients enrolled during March 1, 2007 to December 31, 2007 in Maitama District Hospital.From this population, a total of 1,098 patients comprising 388 patients from General Hospital Minna and 710 patients from Maitama District Hospital were selected using simple random sampling technique. The sample size was determined in a manner to include at least 10% of the study population.[17] The study sites were selected using purposive sampling technique.

Selection criteria

All patients testing positive for HIV who were ineligible to start ART and enrolled into HIV care by registration in the Pre-ART register during the period of interest (May 1, 2007 to December 31, 2007 for General Hospital Minna and March 1, 2007 to December 31, 2007 for Maitama District Hospital) were eligible to be included in the study. All patients testing positive for HIV who were either ineligible to start ART but not registered in pre-ART register or eligible to start ART during the period of interest were excluded from the study.

Outcome variables

The major outcome variables were CD4+ cells count and pre-ART status at the end of observation period. We defined 'ART start' as when a patient in pre-ART care becomes eligible and commenced ART; and 'transferred-out' as when a patient is transferred out (with records) to another health facility to continue pre-ART care. Lost to follow up (LTFU) refers to patients failing two consecutive clinic visits in six-month blocks per year for any unknown reasons; 'dead' refers to patients who were known to have died; while 'active in pre-ART care' refers to those patients who were

current on pre-ART care at the end of observation period.

Ethical Consideration

Ethical approval for this study was obtained from National Health Research Ethics Committee (NHREC), Federal Ministry of Health Abuja Nigeria. Confidentiality was assured by excluding the patients' identifiers during data analysis.

Data collection

Data collection was done using a study-specific and structured data extraction instrument designed to ensure uniformity of the patients' data for analysis. The instrument was used to extract relevant data from the routinely collected clinical, immunologic and outcome data in manually maintained patients' hospital records. The cut-off date for the data extraction was 30th April 2012. Data collection was carried out by the researchers and two trained research assistants over two months period. The researchers and the assistants used patients' identifiers to sort and filter out duplicate registrations and assigned a code to each of the patient's data before data entry. About one-tenth of data extracted from the patients' hospital records were randomly verified from source documents and any discrepancies were reconciled where possible.

Data Analysis

The data was entered into Predictive Analytical SoftWare (PASW) statistics® version 18 for analysis. Descriptive statistics including frequency distribution were used for sample characteristics. The total time of follow up in pre-ART care contributed by each patient was summed up to obtain the total person-years of follow up. The CD4 cells count (cells/mm^3) was grouped into categorical variable; <50, 50 – 149, 150 – 249, 250 - 349 and $\geq$350 cells/mm^3. Paired sample *t-test* and simple linear correlation were used to test the association of the CD4-cell counts at different time intervals. The mean rate of CD4 cells count (cells/mm^3) decline over a time interval was calculated by dividing the change in CD4 cells count (cells/mm^3) over that time period by the time interval. Chi-square was used for inferential statistics. All reported P-values were 2-sided, and $P < 0.05$ used to determine statistical significance.

RESULTS

Socio-demographic characteristics of patients

The mean age of study participants was 33.1 (95% CI, 32.6 – 33.6) years old; 53.4% were aged 30 – 34 years; 65.1% were females and 39.4% were married. Of the participants, 19.9% had secondary level education and 21.0% were employees (Table 1).

Table 1: Distribution ofsocio-demographic characteristics of patients, n = 1098.

Characteristics	Frequency	Percent
Sex		
Male	360	32.8
Female	715	65.1
Not Indicated	23	2.1
Age group (years)		
<15	5	0.5
15 – 29	354	32.2
30 – 44	586	53.4
45 – 59	113	10.3
>59	8	0.7
Not Indicated	32	2.9
Educational status		
None	34	3.1
Primary	108	9.8
Secondary	219	19.9
Post-secondary	193	17.6
Not indicated	544	49.5
Marital status		
Single	201	18.3
Married	433	39.4
Divorced	8	0.7
Widowed	44	4.0
Not indicated	412	37.5
Employment status		
Student	41	3.7
Unemployed	210	19.1
Employee	231	21.0
Self-employed	205	18.7
Retired	7	0.6
Not indicated	404	36.8

Patients' baseline clinical characteristics of the participants, 33.1% and 25.0% had baseline WHO clinical stage III and CD4 cells count of $\geq$ 350 cells/mm^3 respectively. Following the clinical screening for opportunistic infections including tuberculosis (TB), 23.3% of the participants had opportunistic infections (OIs) at pre-ART enrolment and of which 3.8% of them were TB suspects (Table 2). The OIs reported included mainly the signs and symptoms of Herpes zoster, Kaposi sarcoma, Candidiasis, Cytomegalovirus (CMV) and TB amongst others.

Table 2: Distribution of baseline characteristics of patients; n = 1098

Baseline characteristics	Frequency	Percent
Baseline WHO Clinical Stage		
Stage I	362	33.0
Stage II	241	21.9
Stage III	363	33.1
Stage IV	38	3.5
Not indicated	94	8.6
Baseline CD4 cells count (mm^3)		
<50	147	13.4
50 – 149	204	18.6
150 – 249	192	17.5
250 - 349	139	12.7
350 and above	275	25.0
Not indicated	141	12.8
Baseline TB status		
Asymptomatic	831	75.7
TB suspected	42	3.8
TB positive not on drugs	11	1.0
TB treatment	5	0.5
Not indicated	209	19.0
Opportunistic infections (OIs) present		
Yes	256	23.3
No	790	71.9
Not indicated	52	4.7

CD4 Cells Evolution in Pre-ART care

During the 5-year study period, there was a decline in CD4 cells count (cells/mm^3) of the pre-ART patients at the stipulated time intervals except at month 54. These declines were statistically significant at months 3, 6, 12, 18, 30 and 42 ($P < 0.05$) (Table 3). There was a positive correlation of baseline and follow up CD4 cells estimates at the stipulated time intervals (Table 3). The mean yearly and monthly rates of CD4 cells count decline was 2.5 (95% CI, 2.1 – 2.9) cells/mm^3 per annum and 3.4 (95% CI, 2.1 – 4.7) cells/mm^3 per month respectively. Figure 1 shows the CD4 cells evolution of pre-ART patients over the 5-year period.

Table 3: Comparison of baseline and follow up CD4 cells estimates of pre-ART patients over time.

Paired CD4-cells count (cells/mm^3)	Mean (±SD)	N	Paired samples correlation		Paired samples t-test		
			Correlation	p-value	t	df	p-value
Baseline	277.7 (±210.7)						
Month 3	263.5 (±200.3)	207	0.883	**0.000**	2.049	206	**0.042**
Baseline	438.5 (±219.7)						
Month 6	385.1 (±236.3)	132	0.765	**0.000**	3.903	131	**0.000**
Baseline	484.5 (±229.9)						
Month 12	445.4 (±241.6)	92	0.682	**0.000**	1.994	91	**0.049**
Baseline	536.4 (±258.4)						
Month 18	471.9 (±238.0)	47	0.749	**0.000**	2.500	46	**0.016**
Baseline	538.1 (±169.9)						
Month 24	484.9 (±226.0)	41	0.339	**0.030**	1.465	40	0.151
Baseline	546.3 (±163.6)						
Month 30	440.2 (±199.8)	34	0.350	**0.042**	2.957	33	**0.006**
Baseline	549.3 (±134.8)						
Month 36	474.7 (±194.0)	15	0.204	0.467	1.358	14	0.196
Baseline	630.0 (±175.0)						
Month 42	455.9 (±240.6)	12	0.220	0.492	2.280	11	**0.044**
Baseline	588.2 (±195.9)						
Month 48	479.0 (±269.9)	9	0.605	0.084	1.508	8	0.170
Baseline	633.4 (±193.3)						
Month 54	644.6 (±288.6)	5	0.835	0.078	-0.151	4	0.887
Baseline	585.3 (±180.1)						
Month 60	426.7 (±319.2)	9	0.708	**0.033**	2.070	8	0.072

SD, Standard deviation; df, degree of freedom

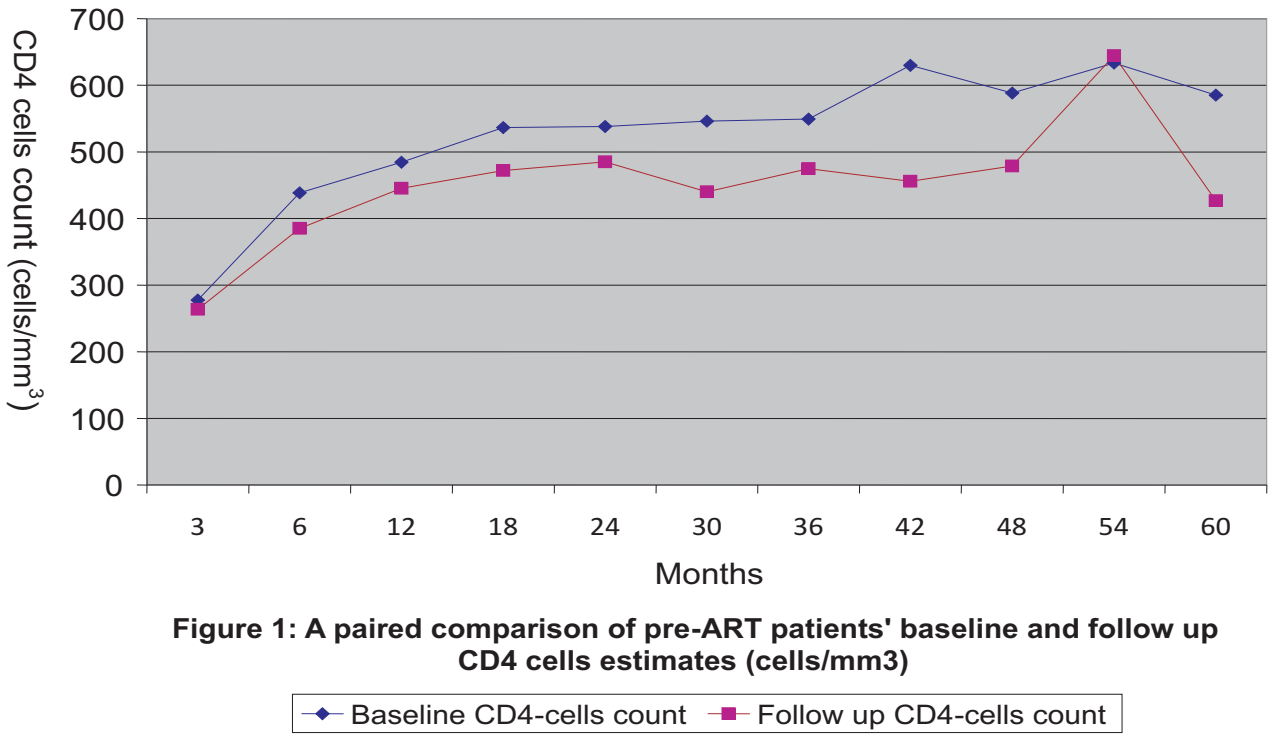

Figure 1: A paired comparison of pre-ART patients' baseline and follow up CD4 cells estimates (cells/mm3)

Pre-ART Outcomes

The patients' pre-ART outcomes included 616 (56.1%) started ART, 436 (39.7%) were lost to follow up, 29 (2.6%) were transferred out, 5 (0.5%) were dead, 10 (0.9%) were still active in pre-ART care while the outcomes were not indicated in 2 (0.2%) of the patients (Table 4). The outcomes of pre-ART care was associated with duration in HIV care (P = 0.000), baseline WHO clinical stage (P = 0.000), baseline CD4 cells count (P = 0.000), baseline TB status (P = 0.000), and presence of opportunistic infections at pre-ART enrolment (P = 0.003).

Of the patients, 275 (25.0%) had baseline CD4 cells count (cells/mm^3) of 350 or greater and out of which 160 (58.2%) were lost to follow up, 97 (35.3%) started ART, while 10 (3.6%) were active on pre-ART care at the end of the study period (Table 4). Of the patients, 38 (3.5%) had baseline WHO clinical stage IV out of which 30 (78.9%) started ART while 7 (18.4%) were lost to follow up. Of the patients, 11 (1.0%) of the patients were TB positive but not receiving anti-tuberculosis drugs at pre-ART enrolment, and out of these 3 (27.3%) were lost to follow up and 8 (72.7%) started ART during the study period. The patients who had opportunistic infections at pre-ART enrolment were 256 (23.3%), out of these 157 (61.3%) started ART and 95 (37.1%) were lost to follow up during the study period. At pre-ART enrolment, 774 (70.5%) of these patients were started on cotrimoxazole prophylaxis, of which 546 (70.5%) started ART and 196 (25.3%) lost to follow up during the study period (Table 4).

Table 4: Distribution of pre - ART outcomes segregated by patients' baseline parameters, n=1098.

	Pre-ART outcomes (%)						
Baseline CD4 cells count (cells/mm^3)	**Dead**	**Loss to follow up**	**Transferred out**	**ART start**	**Active in Pre-ART care**	**Not indicated**	**Total, N (%)**
<50	1 (0.7)	42 (28.6)	5 (3.4)	99 (67.3)	0 (0.0)	0 (0.0)	147 (13.4)
50 – 149	0 (0.0)	34 (16.7)	5 (2.5)	164 (80.4)	0 (0.0)	1 (0.5)	204 (18.6)
150 – 249	1 (0.5)	39 (20.3)	3 (1.6)	148 (77.1)	0 (0.0)	1 (0.5)	192 (17.5)
250 - 349	0 (0.0)	47 (33.8)	3 (2.2)	89 (64.0)	0 (0.0)	0 (0.0)	139 (12.7)
350 and above	0 (0.0)	160 (58.2)	8 (2.9)	97 (35.3)	10 (3.6)	0 (0.0)	275 (25.0)
Not indicated	3 (2.1)	114 (80.9)	5 (3.5)	19 (13.5)	0 (0.0)	0 (0.0)	141 (12.8)
Total	5 (0.5)	436 (39.7)	29 (2.6)	616 (56.1)	10 (0.9)	2 (0.2)	1098 (100)
Baseline WHO Clinical Stage							
Stage I	1 (0.3)	167 (46.1)	10 (2.8)	176 (48.6)	8 (2.2)	0 (0.0)	362 (33.0)
Stage II	1 (0.4)	89 (36.9)	8 (3.3)	142 (58.9)	1 (0.4)	0 (0.0)	241 (21.9)
Stage III	1 (0.3)	106 (29.2)	5 (1.4)	248 (68.3)	1 (0.3)	2 (0.6)	363 (33.1)
Stage IV	0 (0.0)	7 (18.4)	1 (2.6)	30 (78.9)	0 (0.0)	0 (0.0)	38 (3.5)
Not indicated	2 (2.1)	67 (71.3)	5 (5.3)	20 (21.3)	0 (0.0)	0 (0.0)	94 (8.6)
Baseline TB status							
Asymptomatic	2 (0.2)	256 (30.8)	19 (2.3)	543 (65.3)	10 (1.2)	1 (0.1)	831 (75.7)
TB suspected	0 (0.0)	16 (38.1)	0 (0.0)	26 (61.9)	0 (0.0)	0 (0.0)	42 (3.8)
TB positive not on drugs	0 (0.0)	3 (27.3)	0 (0.0)	8 (72.7)	0 (0.0)	0 (0.0)	11 (1.0)
TB treatment	0 (0.0)	2 (40.0)	0 (0.0)	3 (60.0)	0 (0.0)	0 (0.0)	5 (0.5)
Not indicated	3 (1.4)	159 (76.1)	10 (4.8)	36 (17.2)	0 (0.0)	1 (0.5)	209 (19.0)
Presence of Opportunistic infections at pre-ART enrolment							
Yes	0 (0.0)	95 (37.1)	0 (0.0)	157 (61.3)	3 (1.2)	1 (0.4)	256 (23.3)
No	4 (0.5)	316 (40.0)	24 (3.0)	438 (55.4)	7 (0.9)	1 (0.1)	790 (71.9)
Not indicated	1 (1.9)	25 (48.1)	5 (9.6)	21 (40.4)	0 (0.0)	0 (0.0)	52 (4.7)
Cotrimoxazole prophylaxis at Pre-ART enrolment							
Yes	3 (0.4)	196 (25.3)	21 (2.7)	546 (70.5)	7 (0.9)	1 (0.1)	774 (70.5)
No	1 (0.4)	195 (75.9)	3 (1.2)	54 (21.0)	3 (1.2)	1 (0.4)	257 (23.4)
Not indicated	1 (1.5)	45 (67.2)	5 (7.5)	16 (23.9)	0 (0.0)	0 (0.0)	67 (6.1)

The pre-ART outcomes were not significantly associated with patients' age ($P = 0.057$) and sex ($P = 0.597$). However, pre-ART outcomes had significant association with patients' educational status ($P = 0.000$), marital status ($P = 0.000$) and employment status ($P = 0.000$). Of the patients that were loss to follow up, 70.3% had secondary education at the least, 63.0% were married, and 61.7% were either employees or self-employed (Table 5).

Table 5: Distribution of pre-ART outcomes segregated by socio-demographic characteristics

Characteristics	Pre-ART outcomes						Total, N
	Dead	Loss to follow up	Transferred out	ART start	Active in Pre-ART care	Not indicated	
Sex							
Male	2 (40.0)	161 (37.3)	7 (25.9)	189 (31.6)	0 (0.0)	1 (50.0)	360 (33.5)
Female	3 (60.0)	271 (62.7)	20 (74.1)	410 (68.4)	10 (100)	1 (50.0)	715 (66.5)
Age (years)							
<15	0 (0.0)	1 (0.2)	0 (0.0)	4 (0.7)	0 (0.0)	0 (0.0)	5 (0.5)
15 – 29	1 (20.0)	142 (33.6)	14 (51.9)	192 (32.0)	5 (50.0)	0 (0.0)	354 (33.2)
30 – 44	4 (80.0)	233 (55.2)	9 (33.3)	334 (55.7)	4 (40.0)	2 (100)	586 (55.0)
45 – 59	0 (0.0)	40 (9.5)	3 (11.1)	69 (11.5)	1 (10.0)	0 (0.0)	113 (10.6)
>59	0 (0.0)	6 (1.4)	1 (3.7)	1 (0.2)	0 (0.0)	0 (0.0)	8 (0.8)
Educational status							
None	0 (0.0)	24 (7.5)	0 (0.0)	9 (4.1)	1 (20.0)	0 (0.0)	34 (6.1)
Primary	0 (0.0)	71 (22.2)	1 (20.0)	36 (16.3)	0 (0.0)	0 (0.0)	108 (19.5)
Secondary	1(100.0)	112 (35.0)	2 (40.0)	102 (46.2)	1 (20.0)	1 (50.0)	219 (39.5)
Post-secondary	0 (0.0)	113 (35.3)	2 (40.0)	74 (33.5)	3 (60.0)	1 (50.0)	193 (34.8)
Marital status							
Single	0 (0.0)	110 (29.1)	3 (50.0)	84 (28.7)	3 (50.0)	1 (50.0)	201 (29.3)
Married	1(100.0)	238 (63.0)	3 (50.0)	187 (63.8)	3 (50.0)	1 (50.0)	433 (63.1)
Divorced	0 (0.0)	4 (1.1)	0 (0.0)	4 (1.4)	0 (0.0)	0 (0.0)	8 (1.2)
Widowed	0 (0.0)	26 (6.9)	0 (0.0)	18 (6.1)	0 (0.0)	0 (0.0)	44 (6.4)
Employment status							
Student	0 (0.0)	22 (5.8)	0 (0.0)	19 (6.4)	0 (0.0)	0 (0.0)	41 (5.9)
Unemployed	0 (0.0)	118 (31.0)	2 (33.3)	85 (28.5)	4 (66.7)	1 (50.0)	210 (30.3)
Employee	0 (0.0)	125 (32.8)	1 (16.7)	103 (34.6)	2 (33.3)	0 (0.0)	231 (33.3)
Self-employed	1(100.0)	110 (28.9)	3 (50.0)	90 (30.2)	0 (0.0)	1 (50.0)	205 (29.5)
Retired	0 (0.0)	6 (1.6)	0 (0.0)	1 (0.3)	0 (0.0)	(0.0)	7 (1.0)

DISCUSSION

The study evaluated the outcomes and CD4 cells evolution among HIV-positive patients who were ineligible to start ART. During the 5-year study period, there was a statistically significant decline in CD4 cells count (cells/mm^3) among pre-ART patients. The average rate of CD4 cells count decline among these patients was very low compared to higher rates of CD4 cells count decline reported in Asia, North America, Australia and Europe.[4, 8-10] This rate was about ten-fold lower than the estimated decline rates reported in other countries in sub–Saharan Africa.[11-14] The rate of CD4 cell decline in pre-ART patients is highly variable, though it is a poor predictor of the risk of AIDS or death in these patients.[4] Several factors related to nutrition, individual's perception of positive HIV status, quality of pre-ART care, socio-cultural and economic status amongst others might be responsible for the wide variations. However, further study would be necessary to identify specific factors that contribute to these wide regional variations in the rates CD4 cells count decline in pre-ART patients. The knowledge of CD4 cells decline

rates in pre-ART patients is essential in deciding when to commence ART as some treatment guidelines recommend ART initiation given a rapid CD4 cell count decline of >50 to 100 cells/ mm^3 per year.[15-16] The outcomes of pre-ART care were significantly associated with CD4 cells count (cells/mm3), WHO clinical stage and CPT status at the enrolment into HIV care. Majority of patients who had baseline CD4 cells count $\geq$350 cells/mm^3 were lost to follow up. The proportion of pre-ART patients who were lost to follow up was higher (two-fifth) among patients with baseline WHO clinical stage I and II compared to other categories. These groups of patients might seem healthier at enrolment and need to be monitored closely and tracked effectively when they default to improve retention in pre-ART care.

This is the first study that reported CD4 cells decline rate among HIV-positive patients enrolled into pre-ART care in Nigeria to our knowledge. The study involved large number of patients over 5-year period and the pre-ART outcomes were available for most patients. The study findings are likely to reflect the operational reality as the data comes from a programme setting. In this study, there were some limitations that should be acknowledged. Some patients declared lost to follow up might have included undeclared cases of transfers out of patients to other health facilities to continue pre-ART care or unascertained cases of deaths. This might overestimate the measures of effect. There was also a limitation of missing data which may bias the distribution of the study findings especially the sample characteristics. This may affect the generalisation of the study findings.

CONCLUSION

There was a significant decline in CD4 cells count (cells/mm^3) of the pre-ART patients over the 5-year observation period. However, the average rate of CD4 cells count decline per annum among these patients was very low compared to previous reports. The outcomes of pre-ART care were significantly associated with CD4 cells count (cells/mm^3), WHO clinical stage and cotrimoxazole prophylaxis (CPT) status at the pre-ART enrolment. Monitoring and tracking of pre-ART patients defaulting follow up clinic appointments is highly recommended to enhance the outcomes of HIV care.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS, UNAIDS (2011). Global HIV/AIDS Response: Epidemic update and health sector progress towards Universal Access Progress Report 2011. Available at: http://www.who.int/hiv/pub progress_report2011/hiv_full_report_2011.pdf. Accessed 20th July, 2012
2. Federal Ministry of Health, FMOH, (2010[b]), Technical report on 2010 National HIV Sero-prevalence Sentinel Survey among Pregnant women attending ante-natal clinics in Nigeria. Abuja, Nigeria.
3. Federal Ministry of Health, FMOH, (2010). National Guidelines for HIV/AIDS Treatment and Care in Adolescents and Adults, Federal Ministry of Health Abuja, Nigeria. October 2010.
4. Wolbers M, Babiker A, Sabin C, Young J, Dorrucci M, Chêne G, Mussini C, Porter K, Bucher HC. (2010) Pretreatment CD4 Cell Slope and Progression to AIDS or Death in HIV-Infected Patients Initiating Antiretroviral Therapy—The CASCADE Collaboration: A Collaboration of 23 Cohort Studies. PLoS Med 7(2): e1000239. doi:10.1371/journal.pmed.100023
5. Mellors JW, Margolick JB, Phair JP, Rinaldo CR, Detels R, Jacobson LP, Muñoz A. (2007) Prognostic value of HIV-1 RNA, CD4 cell count, and CD4 cell count slope for progression to AIDS and death in untreated HIV-1 infection. JAMA 297: 2349–2350.
6. Egger M, May M, Chene G, Phillips AN, Ledergerber B, Dabis F, Costagliola D, D'Arminio Monforte A, de Wolf F, Reiss P, Lundgren JD, Justice AC, Staszewski S, Leport C, Hogg RS, Sabin CA, Gill MJ, Salzberger B, Sterne JA; ART Cohort Collaboration. (2002) Prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: a collaborative analysis of prospective studies. Lancet 360: 119–129.
7. Mellors JW, Munoz A, Giorgi JV, Margolick JB, Tassoni CJ, Gupta P, Kingsley LA, Todd JA, Saah AJ, Detels R, Phair JP, Rinaldo CR Jr. (1997). Plasma viral load and $CD4^+$ lymphocytes as prognostic markers of HIV-1 infection. Ann Intern Med. 1997;126: 946–954.
8. Ng OT, Lin L, Laeyendecker O, Quinn TC, Sun YJ, Lee CC, Leo YS (2011). Increased Rate of CD4+ T-Cell Decline and Faster Time to Antiretroviral Therapy in HIV-1 Subtype CRF01_AE Infected Seroconverters in Singapore. PLoS ONE 6(1): e15738. doi:10.1371/journal.pone .0015738

9. Anastos K, Gange SJ, Lau B, Weiser B, Detels R, Giorgi JV, Margolick JB, Cohen M, Phair J, Melnick S, Rinaldo CR, Kovacs A, Levine A, Landesman S, Young M, Muñoz A, Greenblatt RM (2000). Association of race and gender with HIV-1 RNA levels and immunologic progression. J Acquir Immune Defic Syndr. 24:218–226.
10. CASCADE Collaboration (2003). Differences in CD4 cell counts at seroconversion and decline among 5739 HIV-1-infected individuals with well-estimated dates of seroconversion. J Acquir Immune Defic Syndr. 34:76–83.
11. Kiwanuka N, Robb M, Laeyendecker O, Kigozi G, Wabwire-Mangen F, Makumbi FE, Nalugoda F, Kagaayi J, Eller M, Eller LA, Serwadda D, Sewankambo NK, Reynolds SJ, Quinn TC, Gray RH, Wawer MJ, Whalen CC (2010). HIV-1 Viral Subtype Differences in the Rate of CD4+ T-Cell Decline Among HIV Seroincident Antiretroviral Naive Persons in Rakai District, Uganda. J Acquir Immune Defic Syndr. 54(2): 180–184. doi: 10.1097/QAI.0b013e3181c98fc0
12. Holmes CB, Wood R, Badri M, Zilber S, Wang B, Maartens G, Zheng H, Lu Z, Freedberg KA, Losina E (2006). CD4 decline and incidence of opportunistic infections in Cape Town, South Africa: implications for prophylaxis and treatment. J Acquir Immune Defic Syndr. 42:464–469.
13. Urassa W, Bakari M, Sandstrom E, Swai A, Pallangyo K, Mbena E, , Biberfeld G (2004). Rate of decline of absolute number and percentage of CD4 T lymphocytes among HIV-1-infected adults in Dar es Salaam, Tanzania. AIDS. 8:433–438.
14. Katubulushi M, Zulu I, Yavwa F, Kelly P (2005). Slow decline in CD4 cell count in a cohort of HIV-infected adults living in Lusaka, Zambia. AIDS. 19:102–103.
15. European AIDS Clinical Society (2009) Guidelines: clinical management and treatment of HIV infected adults in Europe (version 5). Available: http://www.europeanaidsclinicalsociety.org/guidelines.asp. Accessed 20th August 2012
16. Hammer SM, Eron JJ Jr, Reiss P, Schooley RT, Thompson MA, Walmsley S, Cahn P, Fischl MA, Gatell JM, Hirsch MS, Jacobsen DM, Montaner JS, Richman DD, Yeni PG, Volberding PA; International AIDS Society-USA (2008). Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel. JAMA 300: 555–570.
17. Nunnally JC. (1978) Psychometric Theory. New York: McGraw-Hill, Inc.