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Association of Pre-Antiretroviral Treatment Body Mass Index with Cd4$^+$ T-Lymphocyte Immune Reconstitution Among HIV-Infected Adults and Adolescents

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Abstract: Human immunodeficiency virus (HIV) causes acquired immune deficiency syndrome (AIDS), a pandemic causing millions of deaths each year. Management of HIV/AIDS patients rely on antiretroviral treatment (ART) to suppress viral replication and increase CD4$^+$ T-lymphocytes levels and time to disease progression in order to enjoy health lives and reduce transmission of the virus. CD4$^+$ count is an essential tool for initiating and monitoring of ART. CD4$^+$ response depend on; environmental setting where treatment is being offered, individual and population characteristics including; adherence, age, gender, baseline CD4$^+$ cell count and viral load and individuals Basal Metabolic Index (BMI), a measure of patient's nutritional status. This study attempts to provide an updated and clear association of independent variables predicting patient's CD4$^+$ immune reconstitution. This was a retrospective longitudinal study of ART-naive, HIV-infected adults and adolescents initiated on standard first line ART regimen and their CD4$^+$ response followed up for 18 months. Study population included adults and adolescents registered and initiated on standard first line ART regimen, as part of routine comprehensive care program of the Kenyan Government in conjunction with donor partners; USAID, ICAP and EGPAF at Masaba-North Sub-County PSC/CCC. Data obtained within the study period of four years; 2012 to 2015 was analyzed statistical using multilevel mixed effect linear models in STATA for BMI categories of CD4$^+$ level intercept values and other variables coefficients and compared to their reference groups to obtain P values. Repeated measures of ANOVA were used to determine differences in CD4$^+$ mean response between the four intervals of measurement. Results from the study indicate that BMI is an independent predictor of CD4$^+$ lymphocytes immune reconstitution for patients on ART. Age, Gender, and Number of ART interruptions were statistically significant when other variables were accounted for in the model over the 18 months of follow up. BMI and WHO clinical stage were less statistically significant.

Keywords: Body Mass Index, Antiretroviral Treatment, ANOVA

1. Introduction

HIV virus causes AIDS and continues to be the world's most serious health and development challenge. According to the World Health Organization (WHO) there were approximately 35 million people worldwide living with HIV/AIDS in the year 2014, of these 31.8 million were adults and 3.2 million were children (< 15 years old) [1]. The vast majority of people living with HIV are in low and middle-income countries of the sub Saharan Africa region, with

approximately 24.7 million people living with HIV/AIDS [2].

Immunological suppression and disturbance caused by HIV infection is responsible for the decline in CD4$^+$ T-lymphocyte cells count and increase in viral load which are predictive of both morbidity and mortality from AIDS related causes [3]. The WHO statistics estimate that 1.5 million people in the World died in the year 2013 of AIDS related causes, of these 1.3million were adults and 190,000 were children [2]. Even currently despite the advances in our scientific understanding of HIV its prevention and treatment, most people living with HIV or at risk of HIV do not have access to prevention, care and treatment and there is still no cure for the disease. However effective treatment with antiretroviral drugs can increase time to disease progression, suppress viral replication and increase CD4$^+$ T-lymphocyte cells, so that people with HIV can enjoy health lives and reduce the risk of transmitting the virus to others [4]. By 2014 WHO estimated 28.6 million people living with HIV (PLHIV) in the World were eligible for antiretroviral treatment (ART), of these 12.9 million were receiving ARTs of which 11.7 million were in low and middle-income countries, 10.96 million were adults and 740,000 were children [2].

The decision to initiate ART in adults and adolescents relies on clinical and immunological assessment [5], WHO emphasizes the importance of using clinical parameters in deciding when to initiate ART, however it is recognized that the value of clinical staging in decision making of when to initiate and monitor ART is improved by additional information provided by baseline and subsequent (longitudinal) CD4$^+$ T-lymphocyte cell count. CD4$^+$ cell count criteria for ART initiation in adults and adolescents for low and middle-income countries according to WHO 2013 guidelines of 200 – 350 cells/mm^3 is used and <200 cells/mm^{3}are also initiated on ART. In spite of CD4$^+$ T-lymphocyte cell count responding rapidly to antiviral therapy and correlating with clinical outcome evaluation during therapy, the CD4$^+$ cell count shows different responses based on; type of setting were treatment is being delivered, individual and population characteristics that include; adherence, age, gender, baseline CD4$^+$ cell count, opportunistic infections i.e TB, baseline viral load and nutritional status of the patient [6] - which is estimated by calculating the individuals Basal Metabolic Index (BMI) as weight divided by height-squared (kg/m^2).

Poor nutritional status at the start of ART has been identified as a predictor of mortality independent of immune status, while patients who gain weight in the early phase of treatment have improved prognosis. Thus, nutritional support is becoming an integral part of ART programs in the sub-Saharan Africa and various supplement are now widely being used. At present, however there are few studies on BMI association with immune reconstitution among HIV infected adults and adolescents initiating antiviral therapy in resource limited settings. The influence of Age, Gender, and Baseline CD4$^+$ cell count, WHO clinical staging, Number of ART interruptions, and TB status on the BMI association with CD4$^+$ T-lymphocyte immune reconstitution during the first 24 months of antiretroviral therapy is yet to be established. The difference in CD4$^+$ cell reconstitution over treatment follow up period, isn't well established either. This study will provide much of this information. Kenya being part of the countries in the sub Saharan Africa region, has approximately 1.6 million people living with HIV/AIDS by 2014, 1.4 million adults and 190,000 children. Total number of deaths in the year 2013 of HIV/AIDS related causes was estimated at 58,000. The PLHIV needing ART by 2014 in Kenya was estimated at 880,000 of these 656,359 had been initiated on ART; 596,228 were adults and 60,141 children, as per UNAIDS Kenya reports [7].

2. Methods

Study site: This study was conducted at Masaba-North sub-county, Nyamira County.

Study design: A Retrospective longitudinal study of ART-naïve, HIV-infected adults and adolescents initiated on standard first line Anti-Retroviral Treatment regimen and followed up for 18 months. Data was retrieved from the pre-ART and ART registers containing HIV/AIDS patient's information, of the years 2011 to 2014.

Study Population: Study population Included ART-naïve, HIV-infected adults and adolescents initiated on standard first line Anti-Retroviral Treatment regimen, as part of routine comprehensive care program of the Kenyan Government patient support clinic (PSC/CCC) in conjunction with donor partners; USAID, ICAP and EGPAF. Masaba-North Sub-County PSC offers health care services to approximately 1300, active pre-ART and ART initiated patients.

Data collection: The required data was collected from patient files. The data was entered in a database; edited, coded, classified and analyzed.

Data analysis: Analysis was done using multilevel mixed effect linear models in STATA to analyze the BMI Categories CD4+ level intercept values and other model variables coefficients were compared to their reference categories to obtain P values. Repeated measures Analysis of variance was used to determine if there was a difference in CD4+ mean response between the four intervals of measurement.

Ethical considerations: Ethical Clearance to carry out the research was obtained from Kenyatta National Hospital (KNH) and University of Nairobi (UON) Board of Scientific and Ethics Review Committee. Permission was also sought from the coordinator HIV/AIDS Masaba North PSC to Access Data. The data collected from the patient registers was kept anonymous and confidential, patient reference identifiers were removed and anonymous coding numbers assigned.

3. Results

A total of 297 study subjects were considered for the study.

Table 1. *Summary statistics of the observations.*

	Obs	Mean	Std. Dev.	Min	Max
Id	1188	149	85.7721	1	297
months	1188	9	6.71103	0	18
Age	1188	37.9259	8.98344	17	67
Gender	1188	1.72727	0.44555	1	2
weight	1188	59.9815	11.2714	27	124
Height	1188	162.983	7.22322	146	185
BMI	1188	22.6049	3.97269	13.44	45.55
WHOstaging	1184	1.84122	0.83769	1	4
ARTinterups	1188	0.83838	0.64705	0	3
counts	1180	382.607	223.153	2	1559
BMI_group	1188	2.13468	0.63222	1	4

Table 1; data of 297 study subjects was analyzed in the study, four repeated measures were obtained from each subject giving a total of 1188 observations (324 (27.27%) for male, 864 (72.73%) for female). Minimum amount of $CD4^+$ estimated in the study was 2 and a maximum of 1559. The lowest weight of recorded on the study was 27kgs and 124kgs at the highest. The lowest age of patients in the study was 17 years and the highest was 67 years. A minimum estimated BMI from the cohort was 13.44 and a maximum of 45.55.

Table 2. *Gender with BMI category tabulation.*

Gender	categorical BMI				
	1	2	3	4	Total
M	28	272	24	0	324
	2.36	22.9	2.02	0	27.27
F	100	540	184	40	864
	8.42	45.45	15.49	3.37	72.73
Total	128	812	208	40	1,188
	10.77	68.35	17.51	3.37	100

BMI categories; 10.77% (2.36% male 8.42female) of the patients in the sample were underweight, 68.35% (22.90% male 44.45% female) normal weight, 17.51% (2.02 male 15.49 female) overweight, 3.37% (0.00% males 3.37% females) were obese (Table 2).

Table 3. *Gender with ART interruptions tabulation.*

gender	No: of ART interruptions				
	0	1	2	3	Total
M	80	196	44	4	324
	6.73	16.5	3.7	0.34	27.27
F	268	500	88	8	864
	22.56	42.09	7.41	0.67	72.73
Total	348	696	132	12	1,188
	29.29	58.5	11.11	1.01	100

Proportion of patients and their respective number of ART interruptions was as follows; 3 = 1.01%, 2 = 11.11%, 1 = 58.59%, 0 = 29.29% (Table 3).

Table 4. *Gender with WHO clinical stage tabulation.*

gender	WHO clinical stage				Total
	1	2	3	4	
M	104	96	116	8	324
	8.78	8.11	9.8	0.68	27.36
F	396	300	148	16	860
	33.45	25.34	12.5	1.35	72.64
Total	500	396	264	24	1,184
	42.23	33.45	22.3	2.03	100

From the data 42.23% of the patients were classified in WHO clinical stage 1, 33.45% in stage 2, 22.30 in stage 3, and 2.03% in stage 4 (Table 4).

Table 5. *Overall fixed effect linear regression.*

Counts Months	Coef.	Std. Err.	t	P>t	[95% Conf.	Interval]
6	61.51014	12.00253	5.12	0.000	37.95309	85.06718
12	96.22956	12.03311	8	0.000	72.6125	119.8466
18	125.0868	12.0884	10.35	0.000	101.3612	148.8124
Age	0	(omitted)				
2.Gender	0	(omitted)				
WHOstaging						
2	0	(omitted)				
3	0	(omitted)				
4	0	(omitted)				
ARTinterups						
1	0	(omitted)				
2	0	(omitted)				
3	0	(omitted)				
BMI_group						
2	0	(omitted)				
3	0	(omitted)				
4	0	(omitted)				
_cons	312.661	8.491825	36.82	0.000	295.9943	329.3277

Table 5, is the general fixed effect linear regression output of 297 subjects, mean baseline CD4$^+$ estimate from the study when all predicting variables are fixed at a constant is 312.6 (95% C.I; 295.9 - 329.3) with an averagely estimated increase of 61.5 (95% C.I; 37.9 – 81.5) at 6 months, 96.2 (95% C.I; 72.6 – 119.8) at 12 months, 125.1 (95% C.I; 101.3 – 148.8) at 18 months.

Table 6. *Fixed effect linear regression for Underweight BMI category (1).*

Counts Months	Coef.	Std. Err.	t	P>t	[95% Conf.	Interval]
6	122.9688	33.18255	3.71	0.000	57.04582	188.8917
12	160.9199	33.58156	4.79	0.000	94.20424	227.6355
18	203.1851	33.95554	5.98	0.000	135.7265	270.6437
Age	0	(omitted)				
Gender	0	(omitted)				
WHOstaging	0	(omitted)				
ARTinterups	0	(omitted)				
_cons	252.9435	23.51636	10.76	0.000	206.2241	299.6628

Mean baseline CD4$^+$ estimate for underweight category when all predicting variables are fixed at a constant is 252.9 (95% C.I; 206.2 - 299.6) with an averagely estimated increase of 122.9 (95% C.I; 57.0 – 188.9) at 6 months, 160.9 (95% C.I; 94.2 – 227.9) at 12 months, 203.2 (95% C.I; 135.7 – 270.6) at 18 months (Table 6).

Table 7. *Fixed effect linear regression for normal weight BMI category (2).*

Counts Months	Coef.	Std. Err.	t	P>t	[95% Conf.	Interval]
6	61.34653	14.19238	4.32	0.000	33.47357	89.2195
12	100.4942	14.21883	7.07	0.000	72.56925	128.4191
18	130.9334	14.29055	9.16	0.000	102.8677	158.9992
Age	0	(omitted)				
Gender	0	(omitted)				
WHOstaging	0	(omitted)				
ARTinterups	0	(omitted)				
_cons	298.5689	10.04015	29.74	0.000	278.8507	318.2872

Mean baseline CD4$^+$ estimate for normal weight category when all predicting variables are fixed at a constant is 298.6 (95% C.I; 278.9 - 318.3) with an averagely estimated increase of 61.3 (95% C.I; 33.5 – 89.2), 100.5 (95% C.I; 72.6 – 128.4), 130.9 (95% C.I; 102.9 – 158.9) at 6 months, 12 months, and 18 months respectively (Table 7).

Table 8. *Fixed effect linear regression for overweight BMI category (3).*

Counts Months	Coef.	Std. Err.	t	P>t	[95% Conf.	Interval]
6	38.78846	31.91614	1.22	0.226	-24.2648	101.8417
12	55.96154	31.91614	1.75	0.082	-7.09167	119.0147
18	82.55769	31.91614	2.59	0.011	19.50448	145.6109
Age	0	(omitted)				
Gender	0	(omitted)				
WHOstaging	0	(omitted)				
ARTinterups	0	(omitted)				
_cons	373.9231	22.56812	16.57	0.000	329.3377	418.5084

Mean baseline $CD4^+$ estimate for overweight category, fixed effect linear regression model is 373.9 (95% C.I; 329.3 - 418.5) with an averagely estimated increase of 38.8 (95% C.I; -24.3 – 101.8), 55.9 (95% C.I; -7.1 – 119.0), 82.6 (95% C.I; 19.5 – 145.6) at 6 months, 12 months, and 18 months respectively (Table 8).

Table 9. *Fixed effect linear regression for obese BMI category (4).*

Counts Months	Coef.	Std. Err.	t	P>t	[95% Conf.	Interval]
6	-13.7	67.84951	-0.2	0.841	-152.916	125.5157
12	16.3	67.84951	0.24	0.812	-122.916	155.5157
18	-11.5	67.84951	-0.17	0.867	-150.716	127.7157
Age	0	(omitted)				
Gender	0	(omitted)				
WHOstaging	0	(omitted)				
ARTinterups	0	(omitted)				
_cons	466.3	47.97685	9.72	0	367.8596	564.7404

Mean baseline $CD4^+$ estimate for obese category when all predicting variables are fixed at a constant is 466.3 (95% C.I; 367.9 – 564.7) with an averagely estimated change of -13.7 (95% C.I; -152.9 – 125.5), 16.3 (95% C.I; -122.9 – 155.5), -11.5 (95% C.I; -150.7 – 127.7) at 6 months, 12 months, and 18 months respectively (Table 9).

Table 10. *Overall ML random effects linear regression.*

Counts Months	Coef.	Std. Err.	z	P>z	[95% Conf.	Interval]
6	61.51014	11.98111	5.13	0.000	38.02759	84.99268
12	96.44177	12.00831	8.03	0.000	72.90591	119.9776
18	125.4597	12.06034	10.4	0.000	101.8218	149.0975
Age	-2.25341	1.107186	-2.04	0.042	-4.42346	-0.08337
2.Gender	30.79989	22.72355	1.36	0.175	-13.7375	75.33723
WHOstaging						
2	-53.2017	22.29842	-2.39	0.017	-96.9058	-9.49757
3	2.924144	27.08323	0.11	0.914	-50.158	56.00631
4	-82.4053	68.55709	-1.2	0.229	-216.775	51.96409
ARTinterups						
1	-124.36	22.65495	-5.49	0.000	-168.763	-79.9575
2	-129.651	35.22449	-3.68	0.000	-198.689	-60.6119
3	-132.56	96.63621	-1.37	0.17	-321.964	56.84318
BMI_group						
2	-14.2429	31.39537	-0.45	0.65	-75.7767	47.29084
3	24.85462	37.35373	0.67	0.506	-48.3573	98.06659
4	-9.00871	60.63397	-0.15	0.882	-127.849	109.8317
_cons	488.7423	60.76948	8.04	0.000	369.6363	607.8482

Overall Maximum Likelihood random effects linear regression output of 297 subjects, mean baseline $CD4^+$ estimate from the study when all predicting variables are changing with time during follow up is 488.7 (95% C.I; 369.6 – 607.8) with an average change over time for every variable as follows; age = -2.25 (95% C.I; -4.42 – -0.08), gender = 30.8 (95% C.I; -13.7 – 75.3), WHO clinical staging in reference to stage one; stage 2 = -53.2 (95% C.I; -96.0 – -9.5), stage 3 = 2.9 (95% C.I; -50.0 – 56.0), stage 4 = -82.4 (95% C.I; -216.7 – 51.9).

Number of ART interruptions in reference to no interruption; 1 = -124.4 (95% C.I; -168.8 – -79.9), 2 = -129.7 (95% C.I; -198.7 – -60.6), 3 = -132.6 (95% C.I; -321.9 – 56.8). BMI categories in reference to underweight; normal weight (2) = -14.2 (95% C.I; -75.8– -47.3), over weight (3) = 24.8 (95% C.I; -48.3 – 98.0), obese (4) = -9.0 (95% C.I; -127.9 – 109.8).

Table 11. *ANOVA.*

	analysis of variance				
Source	SS	df	MS	F	Prob > F
Between groups	2619168	3	873055.9	18.3	0.000
Within groups	56091808	1176	47697.12		
Total	58710976	1179	49797.27		

One way ANOVA output F (3, 1179) = 18.3, p = 0.000.

	Bartlets Test for equal variance		
Means	0	6	12
6	61.3098		
	0.004		
12	97.2895	35.9798	
	0	0.272	
18	126.31	65.0003	29.0205
	0	0.002	0.648

Comparison of mean CD4 levels by months of measurement.

4. Discussion

This longitudinal study aimed to examine the progress of $CD4^+$ lymphocyte immune reconstitution predicted by baseline BMI among a cohort of patients initiated on antiretroviral treatment. The results indicate an overall starting mean $CD4^+$ count of 312.6 (95% C.I; 295.9 - 329.3) Prob F < 0.0001, with an average estimated increase of 61.5 (95% C.I; 37.9 – 81.5) at 6 months, 96.2 (95% C.I; 72.6 – 119.8) at 12 months, 125.1 (95% C.I; 101.3 – 148.8) at 18 months. BMI categories at ART initiation predicted $CD4^+$ lymphocyte immune reconstitution as follows: For the patients in the underweight category their baseline mean $CD4^+$ count was 252.9 (95% C.I; 206.2 - 299.6), with an average estimated increase of 122.9 (95% C.I; 57.0 – 188.9) at 6 months, 160.9 (95% C.I; 94.2 – 227.9) at 12 months, 203.2 (95% C.I; 135.7 – 270.6) at 18 months. For the normal weight category of patients, their baseline mean $CD4^+$ count increased compared to the underweight category but with a reduced rate of increment over the 6, 12, 18 months measuring intervals; 298.6 (95% C.I; 278.9 – 318.3), with an average estimated increase of 61.3 (95% C.I; 33.5 – 89.2), 100.5 (95% C.I; 72.6 – 128.4), 130.9 (95% C.I; 102.9 – 158.9) at 6 months, 12 months, and 18 months respectively.

The study estimated an increased baseline mean $CD4^+$ count for the overweight category compared to underweight and normal weight categories but with a further reduced rate of increment over the 6, 12, 18 months measuring intervals; 373.9 (95% C.I; 329.3 - 418.5), with an average estimated change of 38.8 (95% C.I; -24.3 – 101.8), 55.9 (95% C.I; -7.1 – 119.0), 82.6 (95% C.I; 19.5 – 145.6) at 6 months, 12 months, and 18 months respectively. The study estimated a high baseline mean $CD4^+$ count for obese category compared to underweight, normal weight and overweight categories but with very low and a negative rate of change over the 6, 12, 18 months measuring intervals; 466.3 (95% C.I; 367.9 – 564.7) Prob > F = 0.9693, with an average estimated change of -13.7 (95% C.I; -152.9 – 125.5), 16.3 (95% C.I; -122.9 – 155.5), -11.5 (95% C.I; -150.7 – 127.7) at 6 months, 12 months, and 18 months respectively.

The rate of $CD4^+$ count change for underweight, normal weight and overweight categories was significant with (Prob F < 0.0001, Prob F < 0.0001, Prob > F = 0.00746) respectively, rate of change for obese category was not significant (Prob > F = 0.9693). This study results concurred with the study done by Kiefer et al. (2011), n = 537. The mean changes in CD4 count from pre ART initiation at 6, 12, and 24 months post initiation were 71 (+-107), 89 (+-109) and 153 (+-135) cells/mL, respectively [8]. And that done by (Palermo et al, 2008) which established relationship between baseline BMI category and CD4 change from baseline; for the 357 subjects with 36 months follow-up, baseline BMI did predict change in $CD4^+$ T-lymphocyte count to month 36 (P = 0.005) [9]. In this model, after adjusting for baseline plasma HIV RNA, $CD4^+$ T-lymphocyte count, age, and race, relative to men with a normal BMI (18.5–25 kg/m^2), underweight men had $CD4^+$ increases that were 94 $cells/mm^3$ lower and overweight and obese men had increases that were 35 and 113 $cells/mm^3$ higher, respectively. It disagrees with Crum-Cianflone et al. (2011), study which established a post diagnosis mean decreases in the white blood cell count as the BMI category increased: -1,068, -590, -458, and -316 $cells/mm^3$ respectively (P < 0.001). Compared to normal-weight persons, those who were obese (P < 0.04) had smaller reductions in the white blood cell counts over time, with similar trends for those who were overweight (P < 0.08) [10].

We fitted an overall maximum likelihood random effects linear regression model that accounted for the effects of; gender, age, WHO clinical stage and number of ART interruptions on $CD4^+$ T-lymphocyte cells count over time. The results indicate an overall baseline mean $CD4^+$ count of 488.7 (95% C.I; 369.6 – 607.8) Prob chi2 < 0.0001, with an average change over time for every variable as follows: For every 1 year increase in age $CD4^+$ count decreases by -2.25 (95% C.I; -4.42 – -0.08) P>|z| = 0.042. Females experienced a better increase in $CD4^+$ count compared to males = 30.8 (95% C.I; -13.7 – 75.3) P>|z| = 0.175, the result agree with the study by Maman et al, (2012) which established that after 1 year on ART, women had $CD4^+$ count 40 $cells/mm^3$ (95% CI 34–46) higher than men [11].

Considering WHO clinical stage 1 as reference; patients in stage 2 had an average $CD4^+$ count decrease with time of -53.2 (95% C.I; -96.0 – -9.5) P>|z| = 0.017 (significant), in stage 3 patients had an average change of 2.9 (95% C.I; -50.0 – 56.0) P>|z| = 0.914 (not significant), and those in stage 4 had an average decrease of -82.4 (95% C.I; -216.7 – 51.9) P>|z| = 0.229 (non-significant).

For the number of ART interruptions, selecting no interruptions (0) as the reference category; subjects with 1

interruption had an average $CD4^+$ count decrease of -124.4 (95% C.I; -168.8 – -9.9) P |z| < 0.0001 (highly significant), those who had 2 interruptions their average decrease was -129.7 (95% C.I; -198.7 – -60.6) P |z| < 0.0001 (highly significant), and those who had 3 interruptions = -132.6 (95% C.I; -321.9 – 56.8) P>|z| = 0.170 (non-significant).

For BMI categories underweight as the reference category; subjects in normal weight had an average $CD4^+$ count change of -14.2 (95% C.I; -75.8– -47.3) P>|z| = 0.650 (not significant), for the overweight they had an average change of 24.8 (95% C.I; -48.3 – 98.0) P>|z| = 0.506 (not significant), and the obese subjects had an average $CD4^+$ count change of -9.0 (95% C.I; -127.9 – 109.8) P>|z| = 0.882 (not significant).

The results of this study indicate that; Age, Gender, and Number of ART interruptions were statistically significant when other variables were accounted for in the model over the 18 months of follow up. While baseline BMI and WHO clinical stage were less statistically significant when other variables were accounted for in the model. Becoming consistent with the study by (Blashill et al, 2013) which found out that the interaction between BMI category and time was non-significant, F (4, 178) = 2.1, p =.09 [12]. And those of the study by (Maman et al, 2012) which concluded that Associations with initial BMI and WHO clinical stage were less strong and did not reach statistical significance when the other variables were accounted in the model after 3 years of ART [11].

The study established statistically significant mean differences between the $CD4^+$ count intervals F (3, 1179) = 18.3, p < 0.0001. A six months interval mean change was statistically significant between baseline (0) – 6 months p = 0.004, but for 6 – 12 months p = 0.0272 and 12 – 18 months p = 0.648 the result was not significant. For >6 months interval (0 – 12, 0 – 18, 6 – 18) mean $CD4^+$ count change was significant (p< 0.0001).

5. Conclusion and Recommendation

5.1. Conclusion

The rate of $CD4^+$ count change for underweight, normal weight and overweight categories was significant with (Prob F < 0.0001, Prob F < 0.0001, Prob > F = 0.00746) respectively, rate of change for obese category was not significant (Prob > F = 0.9693).

Age, Gender, and Number of ART interruptions were statistically significant when other variables were accounted for in the model over the 18 months of follow up. In summary the study established that BMI is an independent predictor of $CD4^+$ lymphocyte cells immune reconstitution for patients on antiretroviral treatment.

5.2. Recommendation

Basal Metabolic Index (BMI) which is a measured as determinant of the patients nutritional status and Since it is a predictor of improved CD4 count, there needs to be put more effort in improving the BMI of PLHIV.

More studies can be done to clearly discuss the association of WHO clinical stage and number of ART interruptions as independent predictors of immune reconstitution, because the resulted in low non-significance when all variables were accounted for in random effects model.

Limitations of the Study

The study being retrospective isn't able to account for the effect of opportunistic infections (TB, Cryptococci meningitis) since the infection periods were occurring at different times thus the infected patients were excluded. Other social variable could not be collected from the patient registers but all the relevant available data is obtained.

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