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Same Day Antiretroviral Therapy Initiation, Prevalence and Co-factors of Advanced HIV Disease in an African Population- A 1 Year Report

Abere Sarah [aω*], Dan-Jumbo Alali [bŀ], Oyan Boma [c#], Eno Gomba [c#], Bawo Michael [d†], Asonye Samuel [e‡] and Alabi Ajibola [f¥]

[a] Department of Internal Medicine, Advanced HIV Disease Program, RSUTH, Nigeria.
[b] Department of Family Medicine, RSUTH, Nigeria.
[c] Department of Internal Medicine, RSUTH, Nigeria.
[d] Pharmacy Department, RSUTH, Nigeria.
[e] RSUTH, Nigeria.
[f] Infectious Disease Unit, Department of Pediatrics, RSUTH, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Advanced HIV disease (AHD) represents a stage of HIV infection characterized by severe immunosuppression and a high risk of mortality. An understanding of the burden and associated risk factors for AHD is important in order to design programs targeted at prevention and treatment with the aim of reducing HIV associated morbidity and mortality. This study set out to determine the prevalence and risk factors for AHD in a tertiary health facility in Southern Nigeria as

[ω] Consultant Physician and AHD Coordinator;
[ŀ] Consultant Physician and ART Coordinator;
[#] Consultant Physician;
[†] Pharmacologist;
[‡] Data Analyst and M&E Specialist;
[¥] Consultant Pediatrician;
**Corresponding author: Email: tamsabere@yahoo.com;*

well as to ascertain the frequency of Same day initiation of Highly Active Antiviral Therapy in AHD patients.

Methodology: This was a retrospective cross-sectional review of data from 419 adults and children diagnosed with AHD seen at the antiretroviral therapy clinic and Emergency department of the Rivers State University Teaching Hospital (RSUTH) over a 1year period. Details including personal bio-data and clinical information were obtained from the HIV registry of the hospital.

Results: Four hundred and nineteen (419) patients were diagnosed with Advanced HIV disease between January 2021- January 2022 with a mean age of 35.8 years. Regarding the co-factors, Sixty- four (29.4%) of the 218 persons tested were positive for tuberculosis while 18(9.2%) of the 196 patients tested for cryptococcus infection were positive. One hundred and forty-eight (148) of the AHD population had CD4 cell count of <200cells comprising 144 (97%) adults and 4(3%) children. AHD, defined by a CD4 count of <200 cells was more prevalent within the age bracket of 40-49years (n=51, 34%) and among females [F:M 81 (55%) vs 67 (45%)]. Majority of the patients presented with WHO stage 3 disease (n=64, 43.2%) closely followed by stage 2 disease (n=47, 31.79%). Stage 4 disease was found in only 2.02%. The overall same day initiation (SDI) of AHD patients was 97% (n=144).

Conclusion: Advanced HIV disease is highly prevalent despite the test and treat approach to care. Interventions aimed at prevention, adherence to therapy as well as early recognition and treatment is paramount in reducing the burden of AHD.

Keywords: Advanced HIV disease; same day initiation of antiretroviral therapy; Rivers State University Teaching Hospital.

1. INTRODUCTION

HIV/AIDS is one of the most significant public health problems all over the world. In 2020, approximately 37.7 million people worldwide were living with HIV, 1.5 million people were newly infected with HIV, 680 000 people died from AIDS-related illnesses and only 28.2 million people had access to antiretroviral therapy as of June 2021 [1,2].

There is, however, a universal obligation to bring to an end, new cases of HIV infections and guarantee that everyone with HIV has access to HIV treatment. Therefore, the Joint United Nations Programm on HIV/AIDS (UNAIDS) set out targets to be achieved by 2025 to end HIV/AIDS as a public health threat by 2030 [3]. The UNAIDS 2025 targets state that: by 2025 95% of people with HIV will know their status, 95% of people with HIV who know their status will be on treatment and 95% of people with HIV on treatment will be virally suppressed. Other targets are that by 2025; 95% of people most at risk of HIV will have access to combination prevention services, 95% of women of reproductive age will have their sexual reproductive health needs met, 95% of people will be able to access services to eliminate parent to child transmission of HIV, 95% of people with HIV who are most at risk of HIV will have access to services to support their overall health, such as care for sexual and gender-based violence, mental health, tuberculosis, and other health conditions [3,4].

Substantial progress has been made in controlling the HIV epidemic in the past years, with a considerable reduction in the rate of occurrence of new cases of the disease. Regardless of the programmatic efforts made to suppress the disease transmission, a significant percentage of people living with HIV still experience adverse disease progression before presenting to the hospital to receive treatment [5]. Late presentation for treatment of HIV is not only associated with higher complications and mortality but also increases sexual and perinatal transmission [6]. The adverse disease progression is known as 'Advanced HIV disease' (AHD). Criteria for classification as an AHD is " CD4 cell count below 200 cell/µl or the presence of WHO HIV clinical stage III or IV disease, during the first presentation for care" [7]. Additionally, all children living with HIV below five years are considered as having AHD [8]. AHD is commonly seen among persons infected with HIV during their first visit for HIV treatment (HAART-naïve) but can occur among HAART-experienced individuals [9].

According to the World Health Organization, about 1 in 3 people living with HIV (PLHIV) present to care with advanced HIV disease (AHD) [10]. Findings from community-based Population HIV Impact Assessment surveys

conducted from 2016–2018 in 9 PEPFAR-supported countries found a prevalence of 11-22% of advanced HIV disease [11]. Since the introduction of "same day ART initiation" (SDI) in 2016 by the WHO, this approach has been adopted by many countries including Nigeria [12]. The same day initiation also known as the 'test and treat strategy' is a new approach to HIV care currently adopted by countries to stop the transmission of HIV infection and to avert new infections by the immediate initiation of Highly Active Antiretroviral therapy (HAART). This approach though saddled with a lot of challenges such as unwillingness to start a lifelong medication suddenly, denial and mistrust of the diagnosis and government policies, faith-based beliefs, fear of discrimination and stigma, poverty, fear of the side effects of the medications and poor awareness of the consequences of delay in treatment initiation [13] is critical to the achievement of vision 90-90-90 by 2030.

In Nigeria, the HIV prevalence is estimated at 1.4% among adults aged 15–49 years. Women aged 15–49 years are more than twice as likely to be living with HIV than men with a prevalence of 0.2% in children aged 0–14 years [14,15]. The national prevalence of AHD in Nigeria is still unknown, however, a review of CD4 test results on the National Data Repository showed that approximately 1 in 3 PLHIV had immunologic AHD and 1 in 6 PLHIV are highly immunocompromised, while the AIDS mortality rate is approximately 0.22 per 1,000 [16].

Advanced HIV disease (AHD) is associated with the occurrence of comorbidities, increased cost of hospital care and higher mortality, usually within the first six months of initiating HAART [17]. In the context of the associated burden of AHD, understanding the magnitude of advanced HIV disease in our healthcare setting and the associated factors that influence its occurrence is vital for resource management, provision of quality healthcare to improve the health status of PLHIV and reduction in mortality.

Nigeria has the second largest HIV epidemic in the world [18]. Amidst an estimated 1.8m persons living with HIV/AIDS in Nigeria with a national prevalence of 1.3% the national and regional Prevalence of AHD remains unknown [19]. However, a 2019 report released by the National HIV/AIDS Indicator Impact Survey (NAIIS) revealed an elevated HIV prevalence rate of 3.8% in Rivers state- a region in Southern Nigeria substantially higher than national prevalence of 1.3% [20]. This survey also reported that only 21% of PLWHIV in Rivers state are on life saving ART [20]. Consequently, the United State Center for Disease Control and Prevention (CDC) contracted the Institute for Human virology Nigeria (IHVN) to bridge this gap through the "Surge Project" which aims at reaching Key populations with HIV testing and treatment.

This study aims to assess the prevalence of AHD among patients who present for HIV treatment at the Rivers State University Teaching Hospital and to identify associated factors influencing the prevalence. We also wish to ascertain the percentage of AHD patients seen at our center who initiated HAART on same day of their enrollment.

2. METHODOLOGY

This is a retrospective study of HIV positive patients seen at the antiretroviral therapy (ART) clinic of the Rivers state university teaching hospital (RSUTH) over a 1 year period (January 2021-January 2022). The RSUTH is a tertiary center of care located in southern Nigeria which is one of the seven major centers for the HIV "Surge Project" in Rivers State, Nigeria. Data from HIV positive individuals receiving care in our facility who has been diagnosed of advanced HIV disease were included in this study. Details including personal bio-data and clinical information will be obtained from the HIV registry of the hospital.

Inclusion and exclusion criteria: This is a retrospective review of data from HIV positive patients who are diagnosed of advanced HIV disease and/or have a CD4 count <200 cells/mm^3 attending the ART clinic or admitted via the accident and emergency of the Rivers state University Teaching Hospital (RSUTH) from Jan 2021-Jan 2022. HIV/AIDS patients who do not meet the WHO definition of Advanced HIV disease were excluded from the study as well as children older than two years who have been receiving ART for more than one year. Also, AHD patients diagnosed before or after Jan 2021-Jan 2022 were not be included in the study.

2.1 Study Design and Method

We collected data on patient demographics including age, sex, date of diagnosis, date of HAART initiation, CD4 cell count, HIV biomarkers, and Opportunistic infection

screening and treatment-including tuberculosis (TB) using Determine™ TB LAM Ag test [21] (the lateral flow urine lipoaribomannan assay) -a point of care rapid screening test that detects the presence of the Mycobacterium tuberculosis cell wall antigen lipoarabinomannan, and Cryptococcus infection using the CrAg lateral flow assay [Crag LFA IMMY®] [22] - a dipstick test for the qualitative or semi quantitative detection of the capsular polysaccharide antigen of the Cryptococcus species complex in serum, plasma or CSF. Screening cascades were constructed based on the WHO Advanced HIV disease Guidelines.

2.2 Data Analysis

Data was assessed using Excel Tool Pak statistical package 2019 version. Data will be expressed as mean ± standard deviation and percentages. Continuous variables will be compared with the students t-test while categorical parameters will be compared with chi-square. Relations among variables were assessed using Pearson correlation coefficient, odds ratio and odds logistic regression analysis. All tests were considered to be statistically significant at the P-value < 0.05.

3. RESULTS

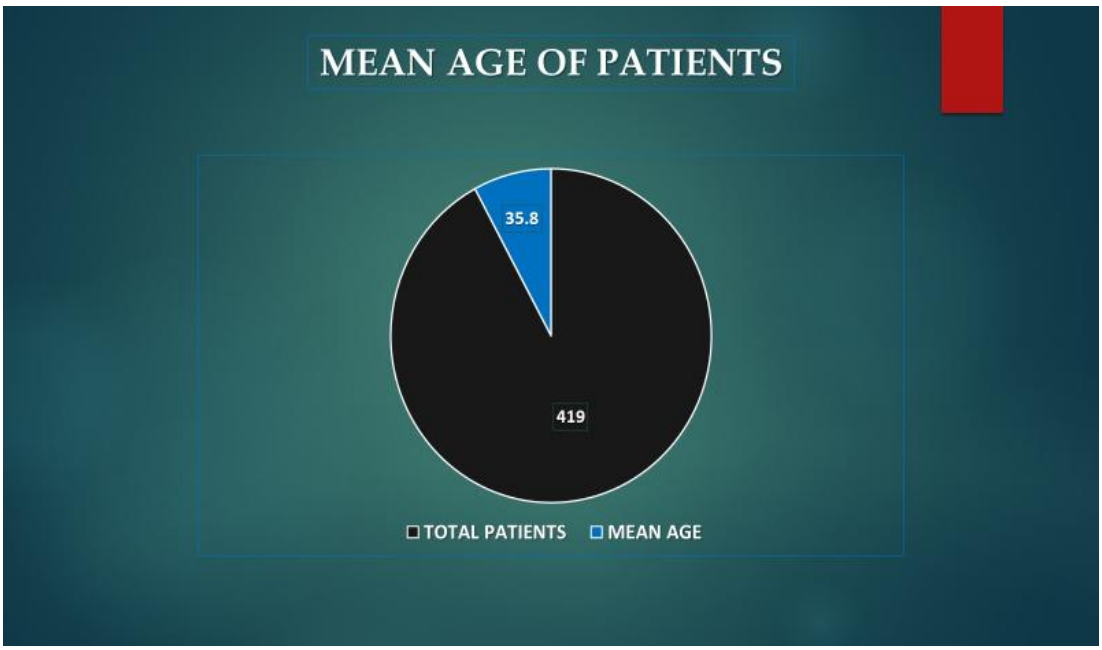
3.1 Clinical Characteristics of the AHD Patients

419 HIV seropositive patients were diagnosed with advanced HIV disease (AHD) in our center between January 2021- January 2022 with a mean age of 35.8 years (Graph 1).

Based on the availability of test kits, enrolled patient had the TB-lam test, CD4 rapid test and CRAG tests done onsite at enrollment and the co-factors of AHD identified were tuberculosis using the urine TB-LAM test and cryptococcal infection via the CrAg LFA test in 64 (29.4%) of 218 AHD patients and 18(9.2%) of 196 AHD patients respectively as shown below.

3.2 Clinical Characteristics of the AHD Patients with CD4<200 Cells

One hundred and forty-eight (148) of the advanced HIV population had CD4 cell count of <200cells/ comprising 144 (97%) adults and 4(3%) children. Comparing the age distribution of the subgroup of the study population with CD4 cells<200 cells/, more patients within the age bracket of 40-49 had CD4 cells <200/ (n=51, 34%). See Fig. 1.



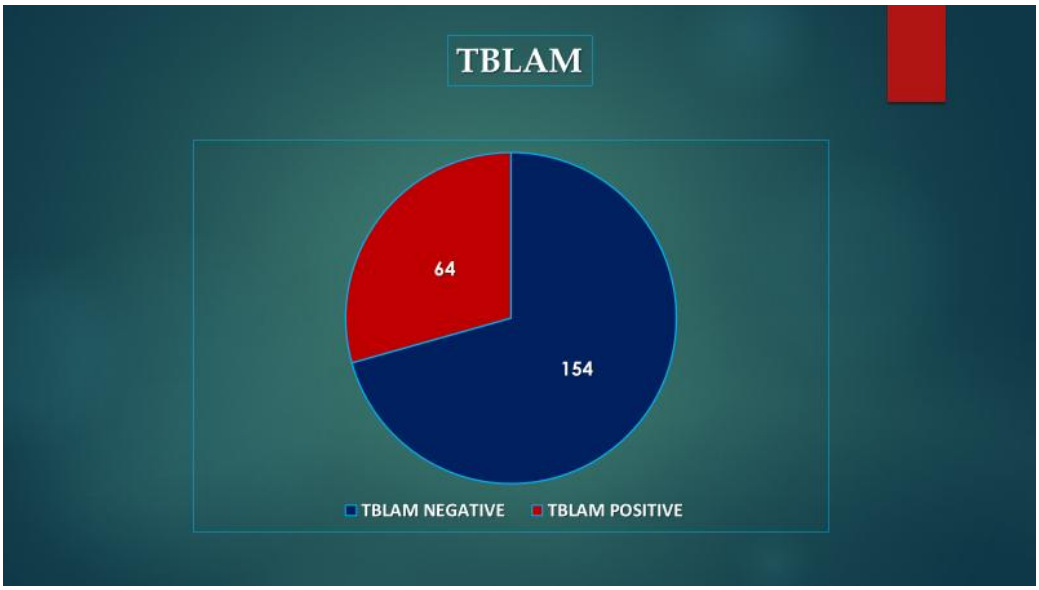
Graph 1. Mean age of the study population

Comparing sexes of AHD patients with CD4<200cells/, we noted that there were more females than males [F:M 81 (55%) vs 67 (45%)] and they were predominantly females within the age group of 40-49 years. Fig. 2.

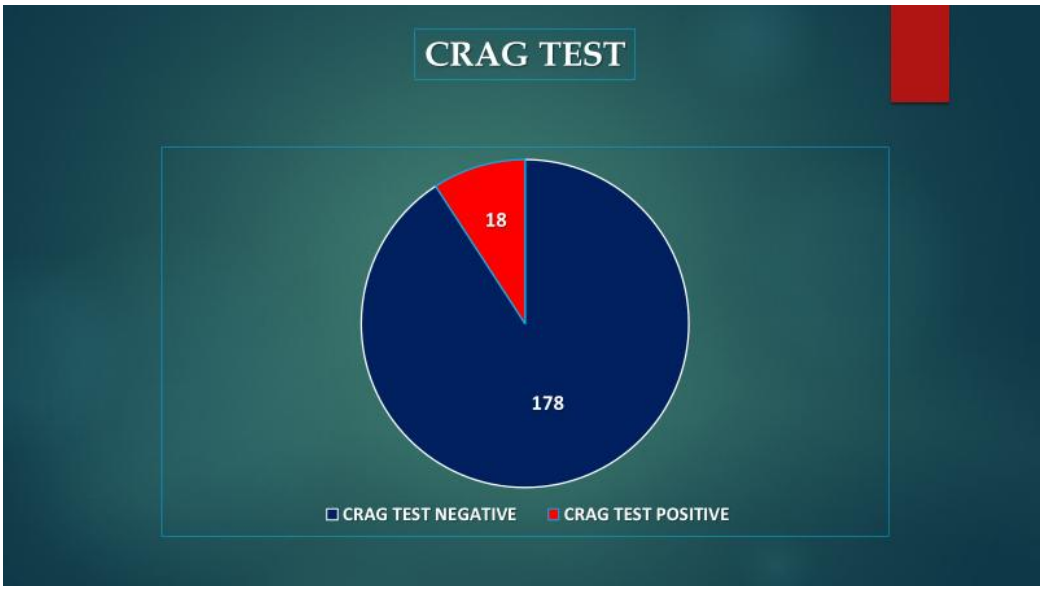
Correlating AHD patients with CD4 cells<200 to the WHO clinical stage of HIV/AIDS, there were more patients with stage 3 disease (n=64, 43.2%) closely followed by stage 2 disease (n=47, 31.79%). There were however fewer patients who presented with WHO clinical stage 4 (2.02%).

3.3 Same Day Initiation of ART (ART Initiation at Enrollment)

The overall same day initiation (SDI) of patients with CD4<200 cells (AHD patients) is 97% (n=144). This means that 144 of the 148 patients with <200 cells CD4 received antiretroviral therapy same day they presented in our facility.



Graph 2. TB- Lam test of the study population



Graph 3. CRAG test in the study population

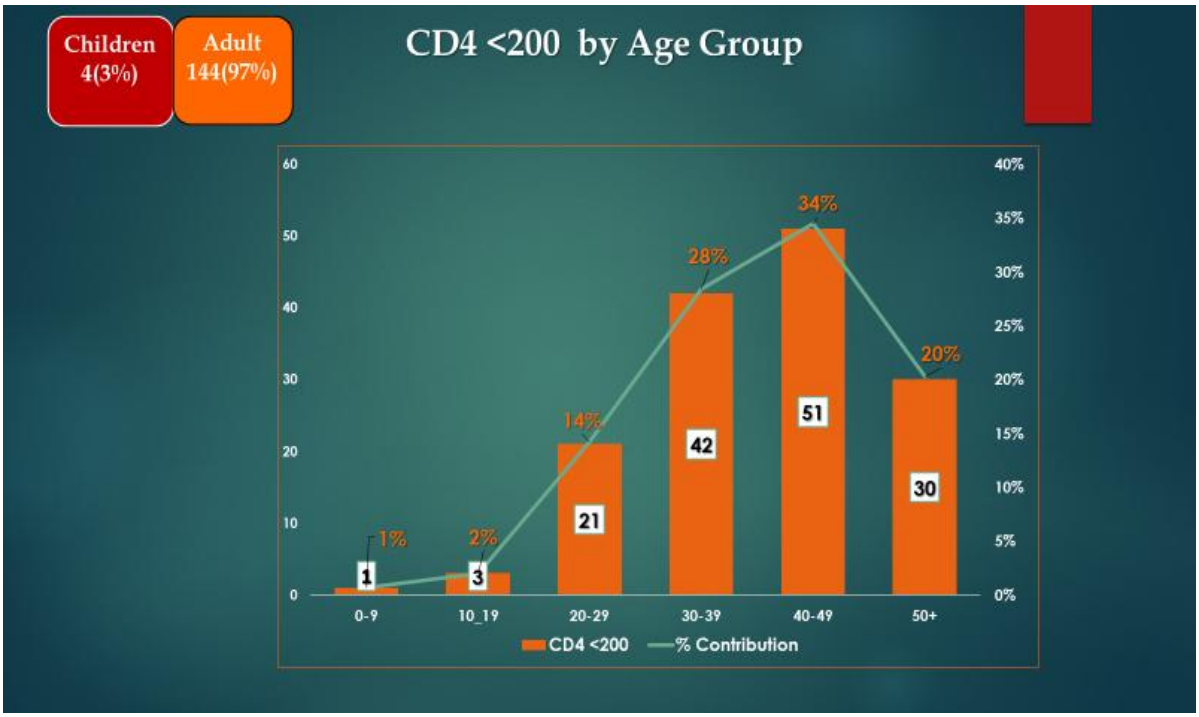


Fig. 1. Age distribution of AHD patients with CD<200 cells

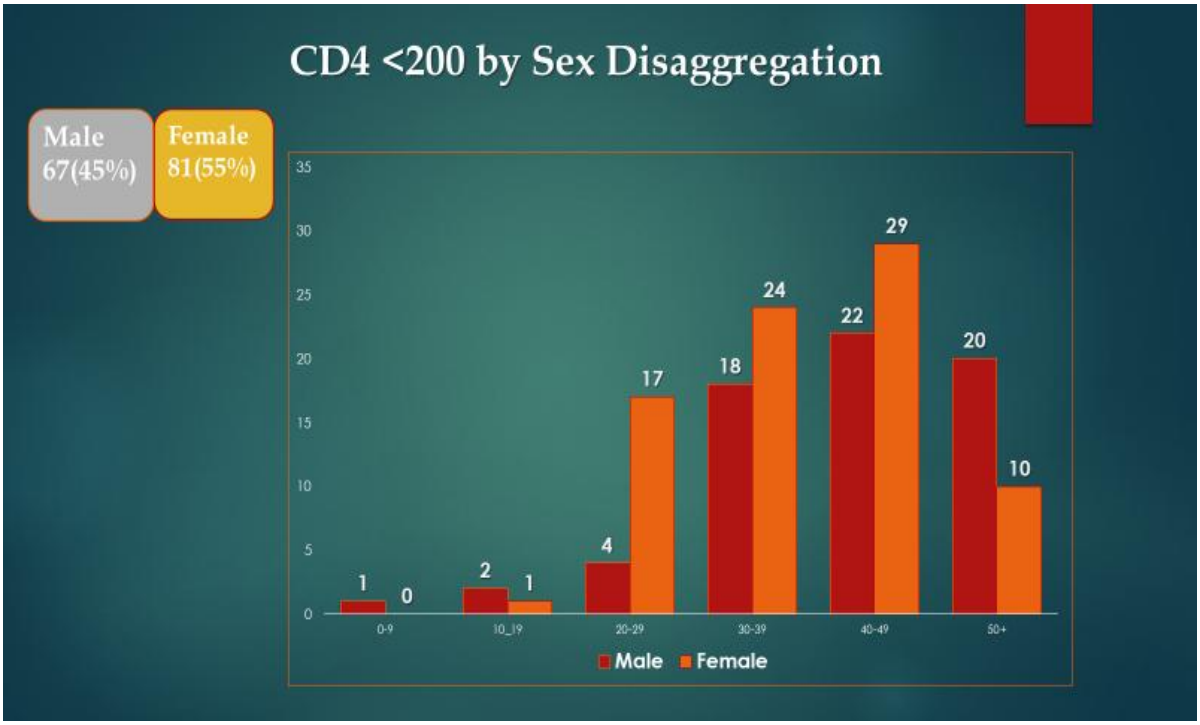


Fig. 2. Male to female of AHD patients with CD4<200 cells

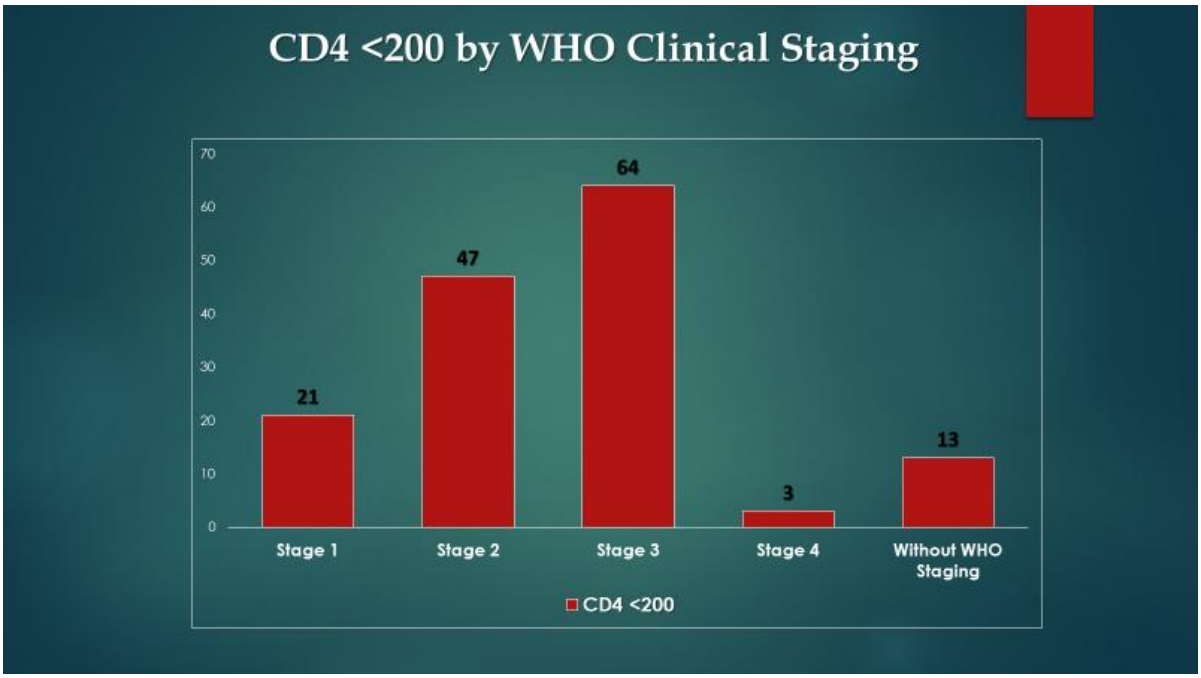


Fig. 3. Correlation of CD cells< 200 cells with WHO clinical stage

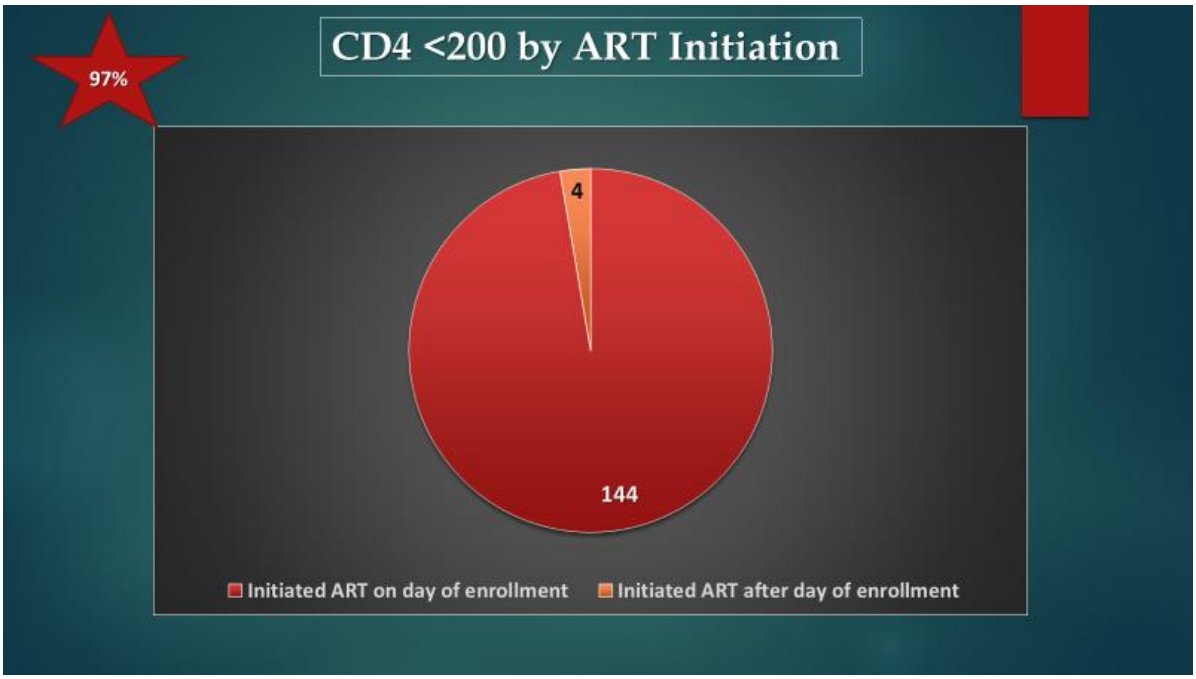


Fig. 4. SDI in AHD population

4. DISCUSSION

This was a 1-year report of AHD program in our facility following the "surge" project in which 419 of 4700 HIV patients seen were found to have advanced HIV disease (Fig. 1) within the research period. According to a WHO recommendation issued in 2015, "all persons living with HIV should commence ART irrespective of their clinical or immune status" [12]. Despite this however, half the population of people living with HIV/AIDS continue to present to care with advanced HIV disease including people presenting to care for the first time

following a HIV diagnosis and people who have treatment failure and consequent decline in CD4 cell count [23].

The mean age of our HIV population who were diagnosed with AHD in study is 35.8 years with a trend towards the younger age group which represents active, independent adult/youths. This trend is not far from that reported by the BEEHIVE study [24,25] - a global open label genetics study of different HIV cohorts. This mean age of 35.8 years also clearly shows that adults are mostly involved in AHD and contact tracing will be required to reduce spread.

Tuberculosis had been a leading cause of death among people with HIV and ranks first amongst opportunistic infections associated with advanced HIV disease [26,27]. WHO recommends rapid diagnostic test and LF-LAM within National Tuberculosis Screening and diagnostic algorithm according to their feasibility, the level of health facility resources and equity [28]. Based on the availability of test kits in RSUTH ART clinic, 218 enrolled patients had their TB test using the TB-LAM of which 64.29% of the patients were positive for TB. Fig. 2.

Cryptococcal disease is one of the most important opportunistic infection among people living with advanced HIV disease and Sub-Saharan Africa share three quarter of the burden [29]. A positive CrAg test was observed in 18 (9.2%) of 196 patients who were tested for cryptococcal infection which though higher than the global prevalence of 6% [30] is similar to reports from other African studies [30,31].

Additionally, access to CD4 count is readily available In RSUTH especially with the availability of point of care technologies and serves as a pre-requisite to enrollment of AHD patient. One hundred and forty-eight (148) of the advanced HIV population had CD4 cell count of <200 cells/ comprising 144 (97%) adults and 4 (3%) children. Comparing the age distribution of the subgroup of the study population with CD4 <200 cells, more patients within the age bracket of 40-49yrs had CD4 count of <200 cells per mm3 of blood (n=51, 34%). This implies that, within the study center (RSUTH), more focus should be on adults in this age bracket for enrollment into AHD package of care to reduce morbidity and mortality.

Correlating the patients with CD4<200 cells to the WHO staging we observed an inverse relationship as a higher number were with WHO stage 2/3 representing over 75% (n=111) of the population. furthermore, 21 (14.2%) were WHO stage 1 despite having CD4 less than 200 cells. Similar findings of low sensitivity of the WHO staging were also observed by Ilovi et al. [32] and Baveewo et al. [33] in their studies validating the WHO staging system.

In our study we observed an overall SDI for patients with CD4<200 cells/mm^3 of 97% (n=144). A high SDI is important in improving HIV care retention, treatment uptake and eventually viral load suppression/reduction in sexual transmission of the disease. A 2019 meta-analysis of over 18011 participants concluded that rapid antiviral therapy initiation in PLWHIV/AIDs improves outcome across HIV treatment cascade [34].

5. CONCLUSION

Advanced HIV disease and its associated opportunistic infections is still highly prevalent despite the test and treat approach to care. Interventions such as the same day initiation of ART which is aimed at prevention, adherence to therapy as well as early recognition and treatment is paramount in reducing the burden of AHD.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval for the study was obtained from the ethical committee of the Rivers State University Teaching Hospital before commencement of the study with clearance number: RSUTH REC 2022170. Ethical issues and processes were addressed regarding data collection, storage, sharing and ownership of data, necessary safeguards for the protection of data and participants.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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