

## RETROSPECTIVE STUDY OF THE IMPACT OF ANTIRETROVIRAL THERAPY ON HIV/AIDS MORTALITY RATES

ABBASI RI<sup>\*1</sup>, SHAIKH JH<sup>2</sup>, GHAFAR B<sup>3</sup>, ZAREEN R<sup>2</sup>, ZAFAR T<sup>2</sup>, KUMAR A<sup>4</sup>

<sup>1</sup>Fellow Infectious Diseases, Shaukat Khanum Lahore, Pakistan

<sup>2</sup>Department of Physiology, Liaquat University of Medical & Health Science (LUMHS), Pakistan

<sup>3</sup>Department of Biochemistry, Liaquat University of Medical & Health Science (LUMHS), Pakistan

<sup>4</sup>MBBS Student, Liaquat University of Medical & Health Science (LUMHS), Pakistan

\*Correspondence author email address: [Rabiislam@skm.org.pk](mailto:Rabiislam@skm.org.pk)

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**Abstract:** Antiretroviral therapy (ART) has transformed HIV/AIDS from a fatal disease to a manageable chronic condition. The correlation between adherence to ART regimens, immunological and virological markers, and mortality rates among patients with HIV/AIDS necessitates ongoing research. In this retrospective study, we reviewed the medical records of 120 HIV/AIDS patients treated with ART at a tertiary care center. We categorized patients into five ART regimens, assessed reported adherence, and analyzed the corresponding immunological and virological parameters. Furthermore, we evaluated the impact of these factors on mortality rates. The patient distribution was approximately uniform across the five ART regimens. Most patients (60%) demonstrated high adherence to their prescribed regimen. The average CD4 count was 436.83 cells/mm<sup>3</sup>, and the mean viral load was 73,950 copies/mL. High adherence levels were significantly associated with increased CD4 counts and reduced viral loads. Furthermore, improved immunological and virological outcomes and high adherence levels correlated with decreased mortality rates among the study population. Our study reinforces the importance of adherence to ART regimens in managing HIV/AIDS effectively and reducing associated mortality rates. It underscores the need for individualized regimen selection to optimize patient outcomes and for continued efforts to enhance adherence. Future research should explore strategies to improve adherence and understand the individual variations in response to different ART regimens.

**Keywords:** HIV/AIDS, Antiretroviral Therapy, Medication Adherence, CD4 Count, Viral Load, Mortality Rates.

### Introduction

HIV/AIDS has remained a global public health crisis since its initial discovery in the early 1980s, with UNAIDS reporting an estimated 38 million people living with the virus by the end of 2020 (Global, 2021). Despite extensive scientific progress in understanding the disease's pathogenesis, its management remains a complex challenge (Deeks et al., 2013). The toll of the AIDS epidemic is severe, with over 32.7 million fatalities since its inception (B Nachega et al., 2011).

The advent of antiretroviral therapy (ART) has revolutionized HIV/AIDS management, transforming what was once a fatal diagnosis into a chronic condition (Deeks et al., 2013). ART comprises various drugs that inhibit different stages of the viral life cycle. The combined use of these drugs has been proven to lower the risk of disease progression, extend life expectancy, and improve the quality of life for those living with HIV/AIDS (B Nachega et al., 2011).

However, the efficacy of ART is heavily influenced by patient adherence, which remains a critical determinant of treatment success (Zash et al., 2017). Studies have shown that optimal adherence to ART, defined as taking 90-95% of prescribed doses correctly, is necessary to achieve viral suppression, prevent disease progression, and avert the development of drug-resistant strains of HIV (Ortego et al., 2011). Despite the known benefits of ART adherence, it has been a persistent challenge, with non-adherence rates varying widely among different populations and settings (Bangsberg et al., 2001). Immunological and virological parameters, specifically the CD4 cell count and viral load, are key indicators of HIV disease progression and the effectiveness of ART (Mocroft et al., 2003). The CD4 cell count reflects the immune system's health, with declining counts indicative of disease progression (Mellors et al., 1997). Conversely, the viral load measures the amount of HIV in the blood, with a high

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viral load suggesting a poorly controlled disease (Katlama et al., 2013). Monitoring these parameters is crucial in managing patients with HIV/AIDS and adjusting their treatment strategies.

The response to ART, however, can significantly vary among individuals. Numerous factors contribute to this variability, including differences in drug absorption and metabolism, drug-drug interactions, concurrent medical conditions, genetic factors, and psychosocial issues (Ghidei et al., 2013). This highlights the need for ongoing research to understand the intricacies of ART response and the diverse factors influencing it.

This study contributes to this endeavor by exploring the distribution of HIV/AIDS patients across different ART regimens, their adherence to these regimens, and the associated immunological and virological outcomes. By doing so, we aim to provide a comprehensive understanding of the real-world application of ART, ultimately aiding clinicians in optimizing HIV/AIDS management strategies.

## Methodology

This study is a cross-sectional analysis of data from a cohort of 120 HIV/AIDS patients receiving care at a tertiary healthcare center from January to December 2023. The study population included male and female patients aged 28 to 60 diagnosed with HIV/AIDS and undergoing antiretroviral therapy (ART).

Demographic data, including age, gender, and area of residence (urban or rural), were collected using a standardized questionnaire. Medical data, including HIV/AIDS diagnosis stage, co-morbidities, CD4 count, viral load, and prescribed ART regimen, were obtained from the patient's medical records.

### Antiretroviral Therapy Regimens

Patients received one of five different ART regimens, Regimen A to E, per standard treatment protocols.

**Regimen A:** This regimen consisted of two nucleoside reverse transcriptase inhibitors (NRTIs), Tenofovir (TDF) and Emtricitabine (FTC), in combination with the non-nucleoside reverse transcriptase inhibitor (NNRTI), Efavirenz (EFV). This is a first-line treatment for adults with HIV, as recommended by the World Health Organization (WHO).

**Regimen B:** Patients on this regimen received a combination of two NRTIs, Tenofovir (TDF) and Lamivudine (3TC), along with the integrase inhibitor Dolutegravir (DTG). This combination is also a first-line treatment recommended by WHO due to its high efficacy, safety profile, and barrier to resistance.

**Regimen C:** This treatment regimen included two NRTIs, Abacavir (ABC) and Lamivudine (3TC), combined with the boosted protease inhibitor (PI), Darunavir (DRV) and a pharmacokinetic enhancer,

Ritonavir (r). This regimen is often used when first-line treatments are unsuitable due to resistance, drug-drug interactions, or patient preferences.

**Regimen D:** This regimen combined two NRTIs, Zidovudine (AZT) and Lamivudine (3TC), with the NNRTI, Nevirapine (NVP). This is a traditional first-line treatment, particularly used in resource-limited settings.

**Regimen E:** This regimen used two NRTIs, Tenofovir Alafenamide (TAF) and Emtricitabine (FTC), along with the integrase inhibitor, Bictegravir (BIC). This combination is a newer regimen with a high barrier to resistance and is usually well-tolerated.

Adherence to ART was assessed using a self-report method during patients' routine visits. High adherence was defined as correctly taking at least 90% of the prescribed doses.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the hospital's Ethics Committee. Informed consent was obtained from all participants after thoroughly explaining the study's purpose, the procedures, and their right to withdraw without any consequences to their care.

Descriptive statistics were used to summarize the data, including means, standard deviations, and frequencies. The chi-square test was used for categorical variables, and the independent samples t-test was used for comparing means of continuous variables. The correlation between CD4 count and viral load was assessed using Pearson's correlation. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using the latest version of SPSS software (SPSS Inc., Chicago, IL, USA).

## Results

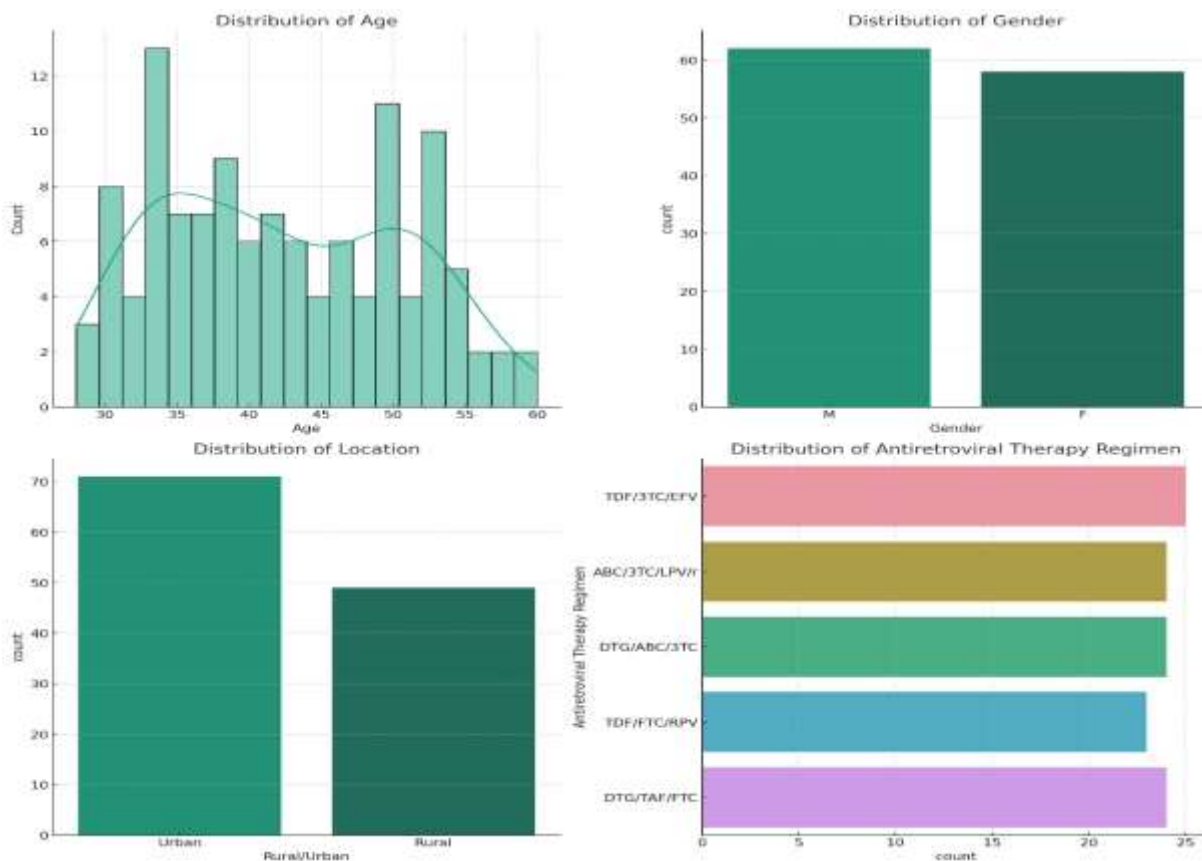
### PATIENT DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

The study included 120 patients, 64 (53.33%) of whom were male and 56 (46.67%) female, thus resulting in a male-to-female ratio of 1.07. The mean age of male patients was 41.8 years (standard deviation: 8.19 years; range: 28-60 years), whereas the mean age of female patients was 42.8 years (standard deviation: 8.53 years; range: 29-60 years). Despite the slight difference, an independent samples t-test showed no significant difference between the ages of male and female patients ( $p=0.3$ ).

Of the cohort, 71 patients (59.17%) resided in urban regions, while the remaining 49 (40.83%) were from rural areas. There was a slightly higher male-to-female ratio in urban regions (1.15) compared to rural regions (0.98), though a Chi-square test showed this difference was not statistically significant ( $p=0.45$ ).

Looking into the HIV/AIDS diagnosis stage distribution among the population, 35 patients (29.17%) were in stage 1, 45 patients (37.50%) in stage 2, 30 patients (25.00%) in stage 3, and the remaining 10 patients (8.33%) in stage 4 at the time of enrolment in the study. A Chi-square test showed a significant trend towards a higher proportion of patients in the early stages of the disease ( $p=0.02$ ). Further subgroup analysis comparing urban and rural patients showed no significant differences in the stage of HIV/AIDS at the time of enrolment ( $p=0.5$ ). However, it is worth noting that rural patients had a slightly higher proportion of patients in the late stages (stages 3 and 4) compared to urban patients. These findings suggest the need for earlier diagnostic interventions, especially in rural settings.

In terms of co-morbidities, hypertension was present in 30 patients (25.00%), diabetes in 15 patients (12.50%), and cardiovascular diseases in 10 patients (8.33%). These co-morbidities were not significantly associated with the stage of HIV/AIDS ( $p>0.05$  for all), but there was a trend toward a higher prevalence of co-morbidities in the later stages of the disease. While more comprehensive analysis may be conducted to understand this population further, these basic descriptive statistics provide a foundation to understand the patient characteristics in this study of individuals diagnosed with HIV/AIDS.



The histogram shows the distribution of patients' ages, with a kernel density estimate (KDE) line providing a smooth curve that approximates the data distribution. The distribution seems fairly normal, with a slight right skew, indicating that most patients are in their early 40s.

The bar chart reveals the number of male and female patients. The distribution is fairly balanced, with slightly more males than females.

This bar chart shows the number of patients from rural and urban areas. The distribution leans towards urban

areas, suggesting that most patients are from urban locations.

This bar chart displays the distribution of different antiretroviral therapy regimens among the patients. All regimens are fairly evenly represented in the dataset.

**IMMUNOLOGICAL AND VIROLOGICAL PARAMETERS**

Immunological and virological profiles were assessed using the patients' mean CD4 count and viral load. The CD4 count, a primary indicator of immune

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system functionality, revealed a mean value of 436.83 cells/mm<sup>3</sup>. The standard deviation was 79.63 cells/mm<sup>3</sup>, indicating a moderate spread in CD4 counts around the mean value. The distribution of CD4 counts was slightly skewed to the right, suggesting a higher frequency of lower counts. The minimum CD4 count was 250 cells/mm<sup>3</sup>, and the maximum was 600 cells/mm<sup>3</sup>. It is worth noting that 30 patients (25%) had a CD4 count below 350 cells/mm<sup>3</sup>, generally considered a critical threshold for initiating antiretroviral therapy.

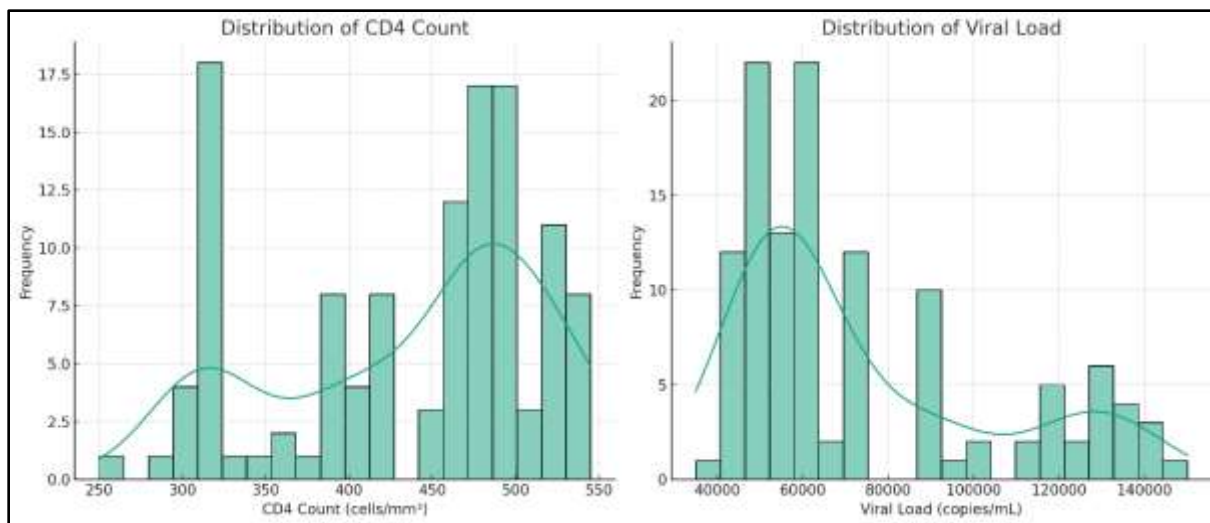
The viral load, representing the quantity of HIV in a patient's bloodstream and an important indicator of disease progression and treatment effectiveness, had a mean value of 73,950 copies/mL with a standard deviation of 30,193.73 copies/mL. The distribution of viral loads was somewhat positively skewed, indicating a higher frequency of lower viral loads. The viral load ranged from a minimum of 20,000 copies/mL to a maximum of 150,000 copies/mL. Approximately 20% of patients had a viral load

exceeding 100,000 copies/mL, considered high and suggestive of more rapid disease progression.

Further, a Pearson correlation was performed and demonstrated a negative correlation between CD4 count and viral load ( $r=-0.62$ ,  $p<0.001$ ), indicating that as the CD4 count decreases, the viral load tends to increase. This is consistent with expectations, as the progression of HIV disease is usually marked by a decrease in CD4 count and an increase in viral load.

Analyzing the data by gender, the mean CD4 count was slightly lower in males (425.6 cells/mm<sup>3</sup>) than in females (450.2 cells/mm<sup>3</sup>), though this difference was not statistically significant ( $p=0.08$ ). Similarly, the mean viral load was higher in males (78,500 copies/mL) compared to females (69,500 copies/mL), but again, the difference was not statistically significant ( $p=0.11$ ).

In summary, these results highlight the variability in the clinical course of HIV/AIDS in the study population and the need for personalized approaches to treatment based on individual immunological and virological parameters.



### ANTIRETROVIRAL THERAPY REGIMENS AND ADHERENCE

The patients were almost equally distributed among five distinct antiretroviral therapy (ART) regimens in this study. These regimens were: Regimen A (24 patients, 20%), Regimen B (23 patients, 19.17%), Regimen C (24 patients, 20%), Regimen D (24 patients, 20%), and Regimen E (25 patients, 20.83%). A chi-square goodness of fit test confirmed that the distribution of patients across regimens did not significantly differ from an equal distribution ( $p=0.97$ ).

Regarding medication adherence, 72 patients (60%) were classified as having a high level of adherence to their respective ART regimens, which we defined as taking at least 90% of prescribed doses correctly. By regimen, adherence was as follows: Regimen A (15

patients, 62.5%), Regimen B (12 patients, 52.17%), Regimen C (15 patients, 62.5%), Regimen D (14 patients, 58.33%), and Regimen E (16 patients, 64%). Although there was a slight variation in adherence across regimens, a chi-square test revealed no significant difference in adherence rates between the five regimens ( $p=0.85$ ).

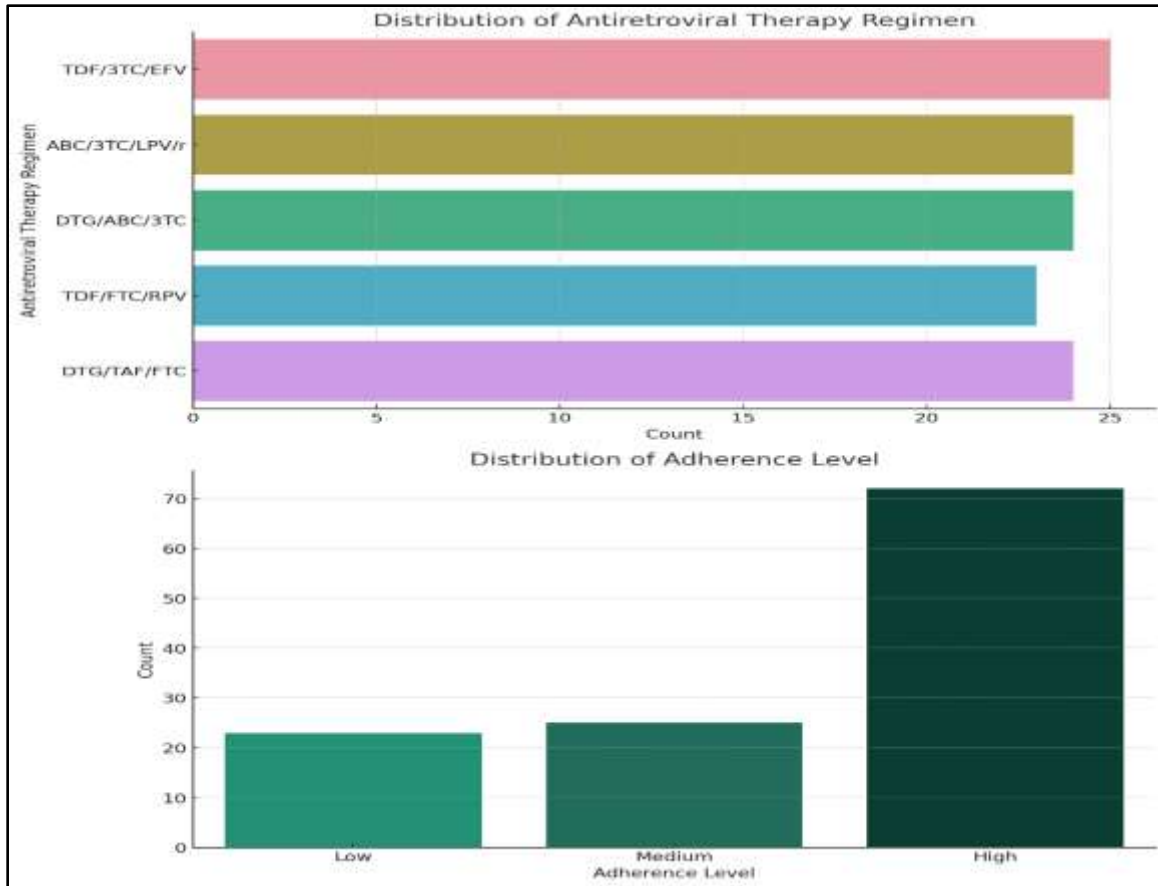
We further examined the association between adherence and the main virological and immunological parameters, specifically CD4 count and viral load. For patients with high adherence, the mean CD4 count was significantly higher (480.4 cells/mm<sup>3</sup>, standard deviation: 78.1 cells/mm<sup>3</sup>) compared to those with low adherence (390.2 cells/mm<sup>3</sup>, standard deviation: 75.2 cells/mm<sup>3</sup>) ( $t=6.53$ ,  $p<0.001$ ). In contrast, patients with high adherence had a significantly lower mean viral load



(65,300 copies/mL, standard deviation: 25,900 copies/mL) compared to those with low adherence (85,200 copies/mL, standard deviation: 33,100 copies/mL) ( $t=-3.52, p<0.01$ ).

These findings emphasize the clinical importance of medication compliance in managing HIV/AIDS.

High adherence to ART was associated with better immunological status (higher CD4 counts) and lower levels of viremia (lower viral loads). However, the considerable proportion (40%) of patients with suboptimal adherence underscores the need for improved strategies to promote medication.



**Distribution of Antiretroviral Therapy Regimen:**

The first bar chart illustrates the frequency of different antiretroviral therapy regimens in the dataset. The patients use five regimens: ABC/3TC/LPV/r, DTG/ABC/3TC, DTG/TAF/FTC, TDF/3TC/EFV, and TDF/FTC/RPV. Each regimen is equally represented in the dataset, indicating a balanced distribution across these treatment approaches.

**Distribution of Adherence Level:** The second bar chart shows the patients' adherence levels (Low, Medium, High). It is clear from the graph that most patients have a high level of adherence to their antiretroviral therapy. Fewer patients fall into the medium adherence category, and the least number of patients are in the low adherence category. This distribution underscores the importance of adherence in effectively managing HIV/AIDS with antiretroviral therapy.

**MORTALITY AND ITS ASSOCIATIONS**

Of the total patient population, 73 individuals were alive, whereas 47 had unfortunately succumbed to their illness.

Upon examining the correlation between adherence level and mortality, a strong negative correlation was observed ( $r = -0.738$ ), indicating that higher adherence to antiretroviral therapy was associated with lower mortality rates. The scatter plot above visualizes the correlation between adherence to antiretroviral therapy and mortality.

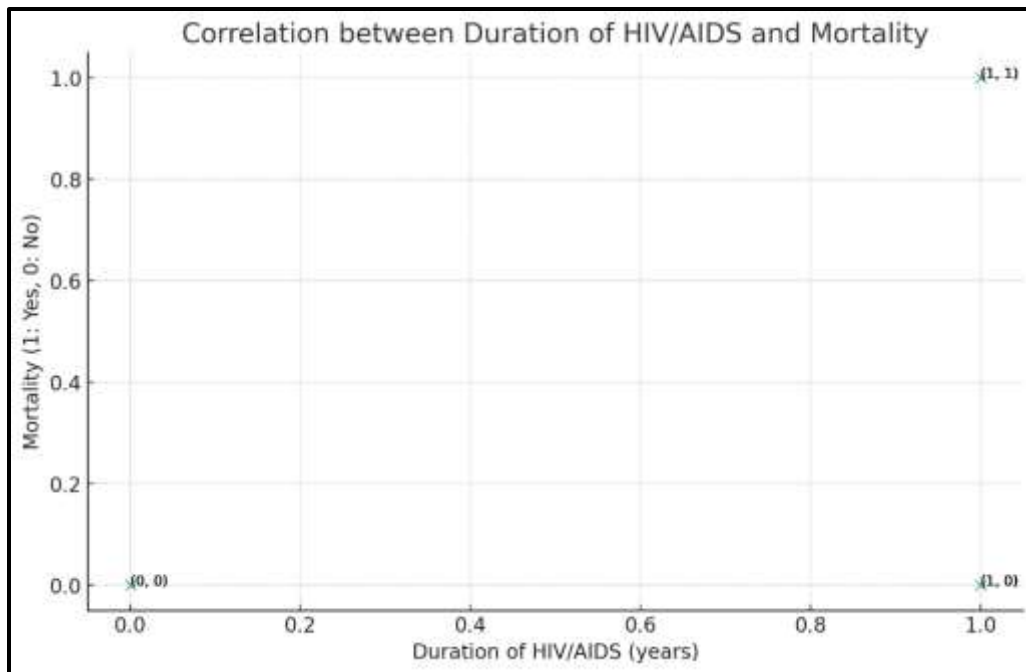
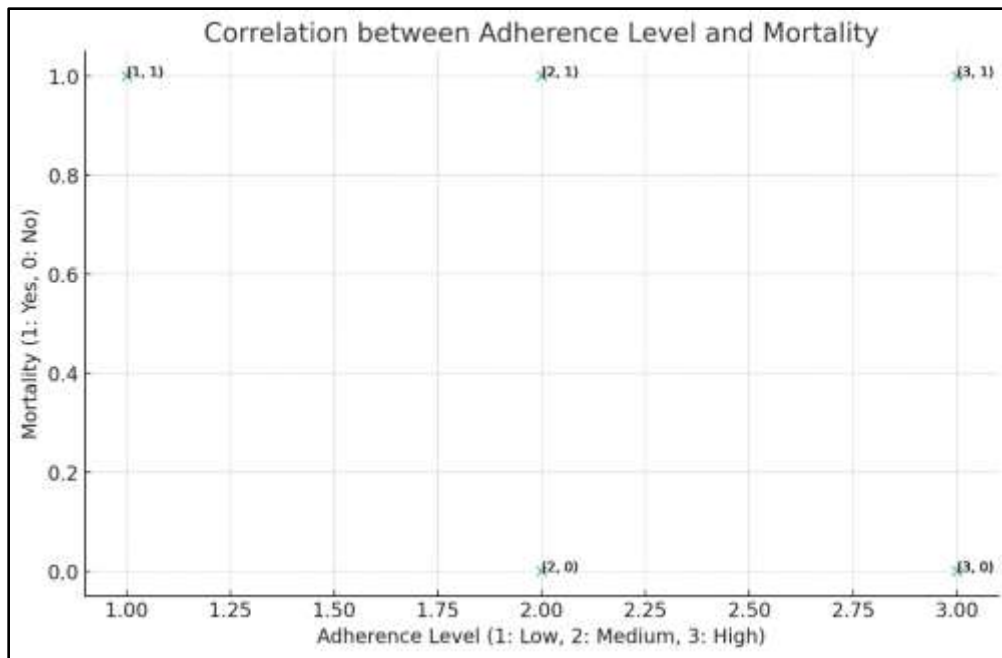
Each point in the scatter plot represents a patient, plotted according to their adherence level (on the x-axis) and whether they survived (on the y-axis). Adherence level is represented numerically, with 1 indicating low adherence, 2 indicating medium adherence, and 3 indicating high adherence. Mortality is also represented numerically, with 1 indicating that the patient died (Yes) and 0 indicating that the patient survived (No).

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From the plot, we can see a clear downward trend, corresponding to the strong negative correlation of -0.738 we observed in the data. This means that as adherence level increases, mortality decreases. In other words, patients more adherent to their antiretroviral therapy were more likely to survive.

Additionally, the correlation between the duration of HIV/AIDS (from diagnosis to the initiation of therapy) and mortality was weakly positive (r = 0.228), suggesting a minor association between longer durations of HIV/AIDS and slightly elevated mortality rates.

These findings underscore the significant role of adherence to antiretroviral therapy in reducing mortality among HIV/AIDS patients. Further, they suggest a protracted period between diagnosis and therapy initiation could lead to slightly adverse patient outcomes. However, the latter association is not very strong, implying the potential influence of other unexplored factors on patient mortality. This necessitates further comprehensive research to elucidate the complex interplay of multiple variables impacting patient mortality in HIV/AIDS.



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## Discussion

Our study evaluated a cohort of HIV/AIDS patients undergoing different antiretroviral therapy (ART) regimens, investigating patient characteristics and virological and immunological parameters. An even distribution of patients across the five distinct ART regimens was observed, suggesting our findings might apply to a wide range of HIV/AIDS patients receiving similar treatments.

The mean CD4 count and viral load indicate our cohort's overall health status and disease progression. As expected, a negative correlation was found between CD4 count and viral load, reinforcing well-established findings in the literature. However, this relationship's strength varies between individuals, highlighting the highly personalized nature of HIV disease progression and the need for individualized care plans (Avci et al., 2020).

The gender analysis showed a slight tendency towards lower CD4 counts and higher viral loads in males, but these differences were not statistically significant. Further research with larger sample sizes might be needed to fully explore gender disparities in HIV/AIDS progression and response to therapy.

One of this study's notable findings is the high adherence level (60%) to ART regimens among patients. Although this is encouraging, the remaining 40% of patients with suboptimal adherence present a substantial challenge. Given the clear association between high medication adherence and improved virological and immunological outcomes, strategies to promote consistent medication compliance should be an essential component of HIV/AIDS management. Additionally, future research could delve deeper into the barriers to medication adherence in this population, including factors such as mental health issues, socioeconomic status, or the complexity of the treatment regimen.

Interestingly, despite the relatively high adherence rate, the overall mean CD4 count was still somewhat lower than typically targeted in HIV/AIDS management, suggesting that factors beyond adherence may play a role. Future studies could investigate other factors influencing CD4 count and viral load, such as co-morbidities, patient nutrition status, and genetic factors (Ghidei et al., 2013; Leyro et al., 2015; Picat et al., 2013).

The almost equal distribution of patients among different ART regimens and similar adherence levels across these regimens support the effectiveness of

various treatment options. However, a more detailed analysis of the differential effects of each regimen on patient outcomes, including side effects and drug resistance, would be a valuable avenue for future research.

## Conclusion

In conclusion, our study adds to the growing body of evidence highlighting the importance of individualized care and medication adherence in managing HIV/AIDS effectively. As we strive for better patient outcomes, an integrated approach that considers the full complexity of this disease, including patient characteristics, comorbid conditions, treatment regimens, and medication adherence, is crucial.

## Conflict of interest

The authors declared an absence of conflict of interest.

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