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# Association of Compliance and Quality the Impact of Antiretroviral Administration During the COVID-19 Pandemic in HIV/AIDS Patients: A Hosptial Based Study in Indonesia

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**Abstract**
Acquired Immune Deficiency Syndrome (AIDS) is a collection of symptoms that arise due to a decrease in the human immune system, caused by the Human Immunodeficiency Virus (HIV). Impact of people living with HIV/AIDS (PLWHA) will experience physical, psychological, social and spiritual problems. Antiretroviral drugs are given to prevent the replication of the HIV virus in CD4 cells, but high adherence is required to achieve suppression of the HIV virus. The aim of this study was to determine the association of compliance and quality with the impact of antiretroviral administration during the COVID-19 pandemic in HIV/AIDS patients. The type of research used is cross-sectional study design. The research sample amounted to 104 PLWHA who carried out control at the polyclinic of Dr. M. Djamil Hospital Padang. The sampling technique used is convenience sampling. The research instrument used was the simplified self-report measure of adherence questionnaire and a study of documentation on the patient's medical record. Data analysis used Chi-square test. $P < 0.05$ was significant, and the data were analyzed using the SPSS version 21.0 program. Most subjects were aged 18-40 years (61.53%) with male (81.7%). The highest educational background was found in high school seniors (49.0%) and married (43.28%). More than half of the subjects were homosexual (45.2%) and family known HIV status (79.9%). A small number of subjects had a history of COVID-19 infection (13.5%) and more than half of the subjects had COVID-19 vaccination status < 2 times (65.39%). Less than half of the subjects had decreased weight gain (18.03%). In subjects who did not comply with taking ARV drugs (23.1%), viral load was not detected (67.3%) and had an increased CD4 cell count (88.5%). The results of the study found that there was a significant relationship with medication adherence with CD4 count, body weight, and viral load ($p<0.05$). It is hoped that health workers will always provide education about the importance of being obedient to taking ARV drugs regularly and support from all parties so that opportunistic infections do not occur, CD4 increases and Viral load is not detected in PLWHA.

**Keywords:** ***AIDS; adherence; COVID-19; PLWHA***

## 1. Introduction

Acquired Immune Deficiency Syndrome (AIDS) is a collection of symptoms that arise due to a decrease in the human immune system, caused by the Human Immunodeficiency Virus (HIV) (Hinkle & Cheever, 2018).

The course of HIV infection in the body attacks Cluster of Differentiation 4 (CD4) cells, resulting in a decrease in the body's defense system (Harding et al., 2020). The most effective way to suppress the number of HIV is to give antiretroviral drugs (ARV), these ARV drugs function to suppress viral replication in CD4 cells (LeMone et al., 2014).

Some people living with HIV/AIDS (PLWHA) are still struggling to comply with ARV drugs due to various challenges, including stress due to daily activities, forgetfulness, drug use disorders, stigma, side effects of ARV (Bezabhe et al., 2016). Other conditions are labeled with chronic illness, especially those associated with HIV stigma, as well as taking regular daily medication with side effects and uncertainty about the future, relationship difficulties, social isolation, and loss of self-esteem. Failure to adjust can in turn lead to clinical depression, anxiety, stress, and poor management. In particular, the prevalence of depression and suicide in people living with HIV/AIDS is very high (van der Heijden et al., 2017).

HIV continues to be a global public health problem, with a global estimate of 38 million people living with HIV and 25.4 million already taking ARV drugs. HIV prevalence in Indonesia is known to be 0.26% in the adult population over 15 years, except in Papua, which has a low-level widespread epidemic with a known prevalence of 1.8% (KEMENKES RI, 2020). The results of the Asian Epidemic Model (AEM) modeling that the peak number of PLWHA is projected to occur in 2019 and new HIV infections will continue to decline between 2019 and 2024 but the number of AIDS-related deaths will continue to increase during this period. The number of PLWHA who had started ARV treatment and were still alive were 211,203 people, with the number of PLWHA who had dropped out or lost to follow-up (LTFU) was 30.77%, and 3.13% were stopping antiretroviral therapy (ART) treatment. The number of HIV/AIDS cases in West Sumatra from January to November 2020 was 367 HIV cases and AIDS was 144 people, the highest percentage of AIDS cases was 30 - 39 years (50.0%). The number of AIDS cases reported by districts/cities in 2020 is the three highest, namely Padang City, Bukittingi City, Pariaman City with a trend of at-risk groups from homosexuals(KEMENKES RI, 2020).

Advances in ART have transformed HIV from a terminal illness to a chronic, treatable medical condition. ART has improved the quality of life of people living with HIV but required daily adherence, adherence still varies between 27% and 80% across different populations in various studies, compared to the 95% required level (Iacob et al., 2017).

At the time of the COVID-19 pandemic, immune deficiency was a risk factor for severe COVID-19 in people with HIV, including the regulation of virological suppression (Hoffmann et al., 2021). HIV remains a significant risk factor for contracting COVID-19 infection and is associated with a higher risk of death from COVID-19. People with HIV need priority consideration for a COVID-19 vaccine (Ssentongo et al., 2021). The results showed that the level of suppression of the undetectable viral load for pre and post-COVID-19 decreased, respectively, the average CD4 count and percentage decreased from pre-covid to post-COVID-19 (Sorbera et al., 2021). CD4 count >200 cells/mm3 pre-COVID-19 and post-COVID-19 decreased.

The study was conducted in 25 countries during 2019 (n=2,389) regarding the prevalence and correlation of suboptimal adherence to ARV therapy in PLWHA, and measured as association with self-reported health outcomes. Overall, 24.1% reported suboptimal compliance, from 10.0% in Austria and 62.0% in China. The most common reasons for skipping ART 5 times in the overall population were feeling depressed/overwhelmed (7.4%), trying to forget about HIV (7.0%) and working (6.1%) (de Los Rios et al., 2020). In addition to harmful physiological effects, research shows that anxiety symptoms and clinical anxiety disorders can affect health outcomes related to ARV treatment adherence, utilization of health services, and quality of life. Growing literature has identified a relationship between anxiety and adherence to ARV therapy (Kemppainen et al., 2013).

Social disruption related to COVID-19 disease threatens to hinder access to regular health services which has the potential to result in interruption of ART treatment, research results show most PLWHA in China are at risk of ART during the COVID-19 outbreak (Sun et al., 2020). The increased psychosocial burden stemming from stress and isolation, as well as, experiencing additional barriers to access to care, can cause them to become more disenfranchised (Waterfield et al., 2021). The aim of this study was to determine the

association of compliance and quality with the impact of antiretroviral administration during the COVID-19 pandemic in HIV/AIDS patients.

## 2. Objectives

The aim of this study was to determine the association of compliance and quality with the impact of antiretroviral administration during the COVID-19 pandemic in HIV/AIDS patients.

## 3. Materials and methods

### 3.1. Study Design and Research Sample

The type of research used is cross-sectional study design. The research sample amounted to 104 PLWHA who carried out control at the polyclinic of Dr. M. Djamil Hospital Padang. The sampling technique used is convenience sampling. The study was conducted in June-December 2021. The study population was HIV/AIDS patients who visited the Voluntary Counseling and Test (VCT) polyclinic at Dr. M. Djamil Hospital Padang during the COVID-19 pandemic. Inclusion criteria were HIV/AIDS patients who had taken ARV drugs for more than 6 months and had CD4 and viral load checks. Data collection in this study looked at the weight obtained by direct measurement using a digital Seka scale, the margin error of the scales was 0.01. Initial laboratory data for CD4, viral load was collected from the results of clinical pathology laboratory examinations of patients in the medical record.

### 3.2. Operational Defenition

Characteristics of respondents in this study were sex (male; female) (Glasner et al., 2022), age (18 - 40 years; 41 - 60 years) (Andini et al., 2019), marital status (married; single; widow) (Andini et al., 2019), risk factor (heterosexual; homosexual; intravenous drugs user), history of COVID-19 infection (yes; no), COVID-19 vaccination status (≥ 2 times; < 2 times) (Lin et al., 2022), starting ARV therapy as seen from the patient's medical record. Adherence to taking ARV drugs using compliance instruments was measured using the Morisky Simplified self-report measure of adherence (Andini et al., 2019), consisting of 4 question items. CD4 count is defined as CD4 levels of patients from laboratory examinations during the treatment period in HIV AIDS patients when starting to receive ARV therapy as seen from the medical record (increased if it was more than the initial CD4 value; decreased if it was same or decreased from the previous unit in mm3), and viral load (detected; not detected) (KEMENKES RI, 2019).

### 3.3. Data Analysis

Univariate analysis was conducted to see the frequency distribution of each variable. The chi-square test was used to determine the association between compliance and quality with the impact of antiretroviral administration during the COVID-19 pandemic in HIV/AIDS patients. $P < 0.05$ was significant, and the data were analyzed using the SPSS version 21.0 program.

## 4. Results

Based research conducted regarding "Association of Compliance and Quality with the Impact of Antiretroviral Administration During the COVID-19 Pandemic in HIV/AIDS Patients: A Hospital Based Study in Indonesia". Obtained the result of Characteristic of respondents (Table 1).

**Table 1: Characteristics of respondents**

| **Variables** | **f (%)** |
|---|---|
| **Age (years)** | |
| 18-40 | 64 (61.53) |
| 41-60 | 40 (38.57) |
| **Sex** | |
| Male | 85 (81.70) |
| Female | 19 (18.30) |
| **Educational background** | |

| | |
|---|---|
| Elementary school | 2 (1.90) |
| Junior high school | 7 (6.70) |
| Senior high school | 51 (49.00) |
| Undergraduate/ Postgraduate | 44 (42.30) |
| **Marital status** | |
| Married | 45 (43.28) |
| Single | 43 (41.34) |
| Widow | 16 (15.38) |
| **Risk factors** | |
| Heterosexual | 47 (45.20) |
| Homosexual | 53 (51.00) |
| Intravenous drugs user | 4 (3.80) |
| **Family known HIV status** | |
| Known | 83 (79.90) |
| Unknown | 21 (20.20) |
| **History of COVID-19 infection** | |
| Yes | 14 (13.50) |
| No | 90 (86.50) |
| **COVID-19 vaccination status** | |
| ≥ 2 times | 36 (34.61) |
| < 2 times | 68 (65.39) |
| **Weight gain** | |
| Increase | 85 (81.70) |
| Decrease | 19 (18.03) |
| **Obedience** | |
| Obey | 80 (76.90) |
| Not obey | 24 (23.10) |
| **Viral load** | |
| Detected | 34 (32.70) |
| Not detected | 70 (67.30) |
| **CD4** | |
| Increase | 92 (88.50) |
| Decrease | 12 (11.50) |

Table 1. found most subjects were aged 18-40 years (61.53%) with male gender (81.7%). The highest educational background was found in high school seniors (49.0%) and married (43.28%). More than half of the subjects were homosexual (45.2%) and family known HIV status (79.9%). A small number of subjects had a history of COVID-19 infection (13.5%) and more than half of the subjects had COVID-19 vaccination status < 2 times (65.39%). Less than half of the subjects had decreased weight gain (18.03%). In subjects who did not comply with taking ARV drugs (23.1%), viral load was not detected (67.3%) and had an increased CD4 cell count (88.5%). Description of antiretroviral treatment interruption (Table 2).

**Table 2: Description of antiretroviral treatment interruption**

| **Antiretroviral treatment interruption** | **f (%)** |
|---|---|
| Yes | 25 (24.03) |
| No | 79 (75.97) |
| Total | 104 (100.00) |

Table 2. shows that from 104 respondents who experienced antiretroviral treatment interruption there were 25 (24.03%). While those who did not experience antiretroviral treatment interruption were 79 people (75.97%). The association between adherence to taking ARV drugs and body weight of PLWHA at the VCT polyclinic (Table 3).

**Table 3: Association between adherence to taking ARV drugs and body weight of PLWHA at the VCT polyclinic.**

| Adherance to taking ARV drugs | Weight | | | | Total | | p-value | OR (95% CI) |
|---|---|---|---|---|---|---|---|---|
| | Increase | | Decrease | | | | | |
| | n | % | n | % | N | % | | |
| Obey | 76 | 95.0 | 4 | 50.0 | 80 | 100.0 | <0.001 | 31.667 (8.617–116.366) |
| Not obey | 9 | 37.5 | 15 | 62.5 | 24 | 100.0 | | |
| Total | 85 | 81.7 | 19 | 18.3 | 104 | 100.0 | | |

Table 3. shows that the results of the analysis of the association between adherence to taking ARV drugs and body weight of 104 PLWHA respondents who obeyed 76 people (95.0%) experienced weight gain ($p < 0.05$) which means there was an association between adherence to taking medication ARV with body weight (OR 31.667, 95% CI 8.617-116.366). The association between viral load and adherence to taking ARV among PLWHA at the VCT polyclinic (Table 4).

**Table 4: Association between viral load and adherence to taking ARV among PLWHA at the VCT polyclinic**

| Viral load | Adherance | | | | Total | | p-value | OR (95% CI) |
|---|---|---|---|---|---|---|---|---|
| | Yes | | No | | | | | |
| | n | % | n | % | n | % | <0.001 | 15.000 (1.652-136.172) |
| Detected | 6 | 22.2 | 21 | 77.8 | 27 | 100.0 | | |
| Not detected | 67 | 95.7 | 3 | 4.3 | 70 | 100.0 | | |
| Total | 73 | 75.3 | 24 | 24.7 | 97 | 100.0 | | |

Table 4. shows that the results of the analysis of the association between viral load and adherence to taking ARV drugs, from 97 complete PLWHA respondents had complete viral load values. Viral load results were undetectable 67 respondents (95.7%) adhered to taking ARV drugs ($p < 0.05$) which means there was an association between viral load and adherence to taking ARV drugs (OR 15.000, 95% CI 1.652- 136.172). The association between adherence to taking ARV drugs and changes in CD4 among PLWHA at the VCT polyclinic (Table 5)

**Tabel 5: Association between adherence to taking drugs and changes in CD4 among PLWHA at the VCT polyclinic**

| Adherence to taking ARV drugs | CD4 | | | | Total | | p-value | OR (95% CI) |
|---|---|---|---|---|---|---|---|---|
| | Yes | | No | | | | | |
| | N | % | n | % | N | % | <0.001 | 66.846 (7.948 – 562.225) |
| Yes | 79 | 98.8 | 1 | 1.3 | 80 | 100.0 | | |
| No | 13 | 54.2 | 11 | 45.8 | 24 | 100.0 | | |
| Total | 92 | 88.5 | 12 | 11.5 | 104 | 100.0 | | |

Table 5 known based on the results of the analysis of the association between ARV adherence and CD4 changes. Of the 104 PLWHA respondents who were obedient, 79 respondents (98.8%) experienced an increase in the CD4 value ($p < 0.05$), which means that there was an association between adherence to taking ARV drugs and changes in CD4 cell count (OR 66.846, 95% CI 7.948 – 562.225)

## 5. Discussion

### 5.1 Characteristics of respondents

The results showed that almost all of the respondents (61.53%) were in the early adult age range (18-40 years). The average age of the respondents was 35 years. The youngest age was 23 years and the oldest was 60 years. The results of this study were the same as those conducted by the Zhejiang Province of China where the majority (79.9%) of HIV AIDS patients were in the age range of 18-40 years. (Liping et al., 2015). Another study in South Africa stated the mean age of ART patients in this sample was 37 years (Wouters et al., 2014). Seen from the average age of HIV/AIDS sufferers. Enter the development of early adulthood, namely at the age of 21-35 years. Early adulthood has work and family roles that require different responsibilities. which can be a source of conflict in the so-called "rush hour" of life. These various social roles can result in the accumulation of stress but can also be a valuable resource for mental health. Overall, combining multiple roles in early adulthood is associated with decreased rather than increased risk for depressive symptoms in older Europeans (Engels et al., 2021).

The results of the study were the same as the research in China as many as 71.3% of the respondents were male (Sun et al., 2020). The results of the study found that men generally showed higher symptoms of depression in developed countries. Based on the most risk factors, homosexuals were 51.0% of the total male respondents (Engels et al., 2021). The increase in the number of PLWHA in the key population is projected only for two sub-groups of the population, namely men like men and male sex workers. The data have shown a fivefold increase in the percentage of HIV case finding among men like men since 2011.

Overall, heterosexual transmission remains the main mode of transmission and the trend is increasing cases from men like men (KEMENKES RI, 2020). Less than half of respondents (24.03%) during the pandemic had experienced antiretroviral treatment interruption (ATI) for more than 1 day. This study was different from previous research, the results showed that most PLWHA in China are at risk of experiencing Antiretroviral Treatment Interruption (ATI) and some have missed taking ARV drugs due to the COVID-19 pandemic (Sun et al., 2020). The results of another study were 25 people (24.03%) who had experienced ATI during the COVID-19 pandemic, which is because of the research time in China at the beginning of the COVID-19 pandemic (Liu et al., 2022).

Less than half of the respondents (23.1%) are known to be non-adherent to taking ARV drugs at the VCT polyclinic. These results are the same as the research conducted in India in 2014 which revealed that of the 85 participants studied. 25% were found to be depressed and non-adherent to ART and in contrast to the study conducted by 47.5% PLWHA who were respondents were all women (Andini et al., 2019; Cook et al., 2014). Regardless of the limit point for optimal compliance. our findings support the principle that optimal adherence to ART is associated with positive clinical outcomes. The optimal adherence threshold for achieving a better virological outcome appears to be wider than the commonly used threshold point (95% compliance). Although patients taking ART should be instructed to achieve 95% compliance. Slightly lower adherence concerns should not preclude prescribing ART regimens in the early stages of HIV infection (Bezabhe et al., 2016).

### 5.2 Association between adherence to taking ARV drugs and body weight of PLWHA at the VCT polyclinic

Weight loss during HIV infection is mainly due to reduced food intake due to reduced appetite. Weight loss and wasting are common among people living with HIV, especially in the late stages of the disease. The incidence of wasting has decreased since the advent of ARVs. Wasting will respond well to ARV therapy, which is the main therapy for wasting in PLWHA. In our study we found the association between adherence to taking ARV drugs and body weight of 104 PLWHA respondents who obeyed 76 people (95.0%) experienced weight gain ($p < 0.05$) which means there was an association between adherence to taking medication ARV with body weight (OR 31.667, 95% CI 8.617-116.366).

These results are in line with those carried out in Nigeria, that the results of the analysis of the relationship between adherence to taking ARV drugs and body weight were 318 PLWHA with an average age of 38 ± 9.6 years and 63% adhered to ART. Obedient clients showed a marked increase in BMI, which means there was a relationship between adherence to taking ARV drugs and body weight (Olowookere et al., 2016).

In contrast to what was done in Africa, the results of t analysis of the relationship between adherence to taking ARV drugs and body weight showed that patients with <80% coverage gained significantly lower body weight than those who were more adherent. but weight gain was not significantly different with adherence rates of more than 80% (Ross-Degnan et al., 2010).

**5.3 Association between viral load and adherence to taking ARV among PLWHA at the VCT polyclinic**

It can be seen that the results of the analysis of the relationship between viral load and adherence to taking ARV drugs. Of the 104 PLWHA respondents whose viral load was undetectable, 67 respondents (95.7%) adhered to taking ARV drugs, which means that there was a relationship between viral load and adherence to ARV taking. These results are in line with those carried out in Nigeria, that the results of the analysis of the relationship between viral load and adherence to ARV medication showed that P 95% reduced viral load to undetectable levels so that there was a relationship between viral load and adherence to ARV medication.

These results are also in line with those carried out in the United States, that overall, 62% (379 of 605) of intervention group participants and 55% (352 of 642) of control group participants achieved undetectable viral load. So, there was a relationship between viral load and adherence to taking ARV drugs (Olowookere et al., 2016).

**5.4 Association between adherence to taking ARV drugs and changes in CD4 among PLWHA at the VCT polyclinic**

Examination of CD4 count is an indicator of immune function because it describes disease progression and life expectancy in PLWHA. This test is also used to assess the immunological response to ARVs and determine the indications for administration and discontinuation of opportunistic infection prophylaxis. PLWHA whose virus has not been detected with ARV therapy even though the CD4 count is between 100 and 200 cells/μL. A high incidence of TB in adult HIV-positive patients is expected, especially in patients with CD4+ T cell counts <200 cells/mm3. Therefore, early HIV screening and ART initiation, as well as strict adherence to ART and increasing coverage of TB preventive therapy to more at-risk groups are needed (Geremew et al., 2020). It can be seen that the results of the analysis of the relationship between adherence to taking ARV drugs and CD4 changes. of 104 PLWHA respondents who were obedient, 79 people (98.8%) experienced an increase in CD4 values, which means that there was a relationship between adherence to taking ARVs and changes in CD4 cells.

These results are in line with those carried out in Nigeria, that of 318 people living with HIV showed a relationship between ART adherence and CD4 cell counts, respondents at three months experienced a higher CD4 count, which means there was a relationship between adherence to taking ARV drugs and changes in CD4 cell count (Olowookere et al., 2016).

These results are also in line with those carried out in South Africa, that out of 109 respondents (94.0%) had an initial CD4 cell count of less than or equal to 200 cells per mm. While 7 respondents (6.0%) had an initial CD4 count of more than 200 cells per mm3. The change in CD4 cell count was calculated as the difference between the initial count (before starting ART) and the most recent count. The lowest baseline CD4 cell count was 2 cells per mm3 and after ARV treatment. The highest was 500 cells per mm3. This means that there was a relationship between adherence to taking ARV drugs with changes in CD4 (Ndubuka & Ehlers, 2011).

Viral load testing can be used to detect treatment failure early and accurately compared to monitoring using immunological and clinical criteria. In addition, viral load examination can also be used as information in deciding to change the combination from first line to second line and so on so that clinical outcomes can be better. Strategic Timing of Antiretroviral Therapy (START) and Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa (TEMPRANO) show the best time to start ARV therapy. In the TEMPRANO study, patients with CD4 cell count >500 cells/μL or any CD4 cell count who immediately started antiretroviral therapy and isoniazid prophylaxis (INH) for 6 months had a lower risk of severe disease than patients who delayed antiretroviral therapy. Whereas in the START study, patients who started antiretroviral therapy at a CD4 cell count >500 cells/μL had a lower risk of severe clinical events belonging to AIDS or non-AIDS than those who started at a CD4 cell count(Group, 2015).

One study found that as many as 70% of patients taking first-line ARVs with a high viral load experienced a decrease in viral load following adherence intervention. Viral load is also used to estimate the risk of transmission to others, especially in pregnant PLWHA and at the population level. Viral load examination was carried out with 2 strategies, the first was routine examination and limited examination. In the routine viral load screening strategy, checks are performed at 6 months after starting treatment, then 12 months after treatment and thereafter every 12 months.

## 6. Conclusion

Most of the respondents adhered to taking ARV drugs. less than half of the respondents during the pandemic had missed taking medication for more than 1 day. There was an increase in weight. The CD4 cell count increased and the viral load was undetectable in the respondents after adhering to antiretroviral drugs. There was a relationship between adherence to taking ARV drugs with body weight. There was a relationship between adherence to taking ARVs with CD4 and a relationship between adherence to taking ARVs and viral load.

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