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Impact of Highly Active Antiretroviral Therapy Regimens on Adherence Among HIV-Infected Attending An HIV-Clinic in A Public Setting in South Africa

KEYWORDS: South Africa; Highly Active Antiretroviral therapy, ARV-adherence; HIV-infected, ARV-regimens

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ABSTRACT *Highly Active Antiretroviral Therapy regimens especially the three-drug regimens that include Protease Inhibitors in combination with nucleoside analogues produce a greatly increased level and long-term suppression of HIV-replication, thus reducing morbidity and mortality associated with the infection. The aim of this study was to determine the impact of ARV-regimens on adherence among HIV-infected attending a primary health care centre in Mthatha, Eastern Cape, South Africa. Data were collected from 86 HIV-infected during a descriptive-cross-sectional study using a standardized-questionnaire and face-to-face-exit interviews. Pill-counts technique was performed and adherence-rate of ≥95% considered acceptable. Data were analyzed using SPSS 22.0. Univariate-factors associated with poor-adherence to HAART were assessed using ANOVA and p≤0.05 considered statistically significant. Of 86 HIV-infected patients, 73.3% were females and 26.7% males with mean age (±SD) of 35.6 (±9.6) years and were enrolled on HAART for 35.5 (±31.8) months. Adherence-rates computed from 32 patients revealed 71.9% having poor adherence-rate. The mean CD4-count at the initiation of HAART was 232.4 (±169.2) cells/mm3, while the latest was 433.7 (±242.9) cells/mm3. Thirty-two (37.2%) patients on Lamivudine, Tenofovir and Efavirenz (regimen 1A-TDF) and 24 (75%) had poor adherence-rate. The commonest adverse effects experienced by patients on regimen 1A-TDF and TDF, Emtricitabine and Efavirenz (regimen FDC) were CNS-related (35.3%) followed by ENT (23.3%). Evaluated variables associated with poor-adherence to HAART were: salary ≥ R2000 (χ2=4.3, p=0.043); WHO-staging 2 and 3 (χ2=12.09,p=0.007) and total number of other tablets (≥4 combined tablets) (χ2 =10.81,p=0.029). Despite an observed overall improvement of patients' immune response following HAART, poor-adherence remains a major challenge due to ADEs associated with regimen 1A-TDF, FDC and burden of ≥4 combined tablets.*

Introduction

The benefits of highly active antiretroviral therapy (HAART) in the management of HIV-infected patients are well established. HAART has been shown to improve CD4-cell counts and Viral loads, thus decreasing morbidity and mortality among HIV-infected patients through the suppression of plasma HIV-1 RNA. The aim of this investigation was to evaluate the impact of Highly Active Antiretroviral Therapy Regimens on Adherence and the treatment response of HIV-infected patients receiving HAART from a primary Healthcare clinic in South Africa.

Background

There has been a substantial improvement in the survival of HIV-infected persons due to the introduction of antiretroviral therapy (ART) and multidrug regimens, or highly active antiretroviral therapy (HAART). The introduction of HAART resulted from the advances in the knowledge of HIV pathogenesis and viral load monitoring.[1] HAART regimens especially the 3-drug regimens with a Protease Inhibitor (PI) in combination with Nucleoside analogues produce a greatly increased level and long-term suppression of HIV replication, thus reducing morbidity and mortality associated with the HIV-infection.[2]

According to Hansan et al.[3] the complexity of these drug regimens alongside issues of toxicity, side effects, disruptions to patient's daily life and difficulties in returning for scheduled follow-up consultations, often makes maintaining adherence over the long term challenging yet the individual and public health benefits of ART are adherence dependent. Inadequate adherence results in antiretroviral (ARV) agents not being maintained at sufficient concentrations to suppress HIV replication in infected cells to lower the plasma viral load. In addition, suboptimal adherence can accelerate development of drug-resistant HIV and mitigate ART's role in reducing HIV incidence and transmission.[4-5]Therefore it is important to promote adherence as these treatments become increasingly available and affordable for people living with HIV (PLHIV) in developing countries where viral load monitoring is not usually possible. Consequently, more attention is being focused on issues related to ART adherence.

The importance of ART adherence makes accurate compliance assessment essential for effective and efficient therapy and evaluation of treatment regimens.[6-7] Authors [8-10] in their studies stated that there are a number of key issues in the study of ART adherence including having an accurate measure of adherence. According to Paterson's pioneer study,[6] adherence up to 95% is necessary for effective HIV-viral suppression.

Understanding the factors that affect non-adherence could provide valuable information about patients most at risk. Stone et al.[11] and Schneider et al.[12] in their studies suggested that factors associated with adherence can be grouped under four main categories: patient factors, for example demographic characteristics,[11] psychological parameter knowledge, personal skills, treatment regimen-related factors such as years on treatment, pill burden, side effects; provider-related factors including the patient-provider relationship.[13] Others are related to environmental and social factors such as supervision of treatment, HIV-related stigma and social support.[9,14]

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According to some authors Malta et al.[10] and Sabin et al.[11] while some factors determining non-adherence to ART may be similar across countries, others may be highly contextual, and culture or country specific. Most ART adherence studies have been undertaken in high-income countries. [8-11] Few studies have assessed adherence rates or predictors in low-or lower-middle income countries.

According to UNAIDS 2012, Sub-Sahara Africa has the highest HIV-infected with SA having the highest prevalence (6.4 million) of HIV/AIDS as compared to other countries in the world with 1:5 people infected. Of these, 80% of 20-24 yrs of HIV-infected are women and 33% of 25 – 29 years are men. In SA 2.6 million people are on HAART with 2500 patients are on HAART in study setting due to the Task shifting Model in HIV care.[15]

Most ART adherence studies have been undertaken in high-income countries.[8,16] Few studies have assessed adherence rates or predictors in low-or lower-middle income countries. The impact of Highly Active Antiretroviral Therapy Regimens on Adherence Among HIV-infected patients attending an HIV-Clinic in a Public Setting in SA, the Eastern Cape has not been reported. Therefore the aim of this study was to determine the impact of ARV regimen on adherence among HIV- infected patients attending a primary health care centre in Mthatha, Eastern Cape, South Africa.

Methodology

Study setting

This study was conducted one of the primary health-care center (PHC) in Mthatha, Eastern Cape, in South Africa. This PHC is among those accredited to roll-out ARVs, therefore one of the site providing free ARVs and related health care services. This facility was selected as it is the most established clinic providing ARV with a pool of HIV-infected patients on ARVs and was willing to participate in the study. At the time of the study, they were 2500 HIV patients registered and receiving ARV medicines.

Study design and participants

This was a descriptive prospective cross-sectional study performed in 2013. Participants in the study were PLHIV receiving free ART provided by the HIV/AIDS care unit. To be included in the study participants had to be 18 years or over and willing to participate in the study. The clinical condition of the patient had to be suitable for ART based on the CD4 count and to be in the WHO clinical stage for at least three months. The PLHIV were responsible for how and when to take the medicine.

Sampling methodology

A convenient sampling method was used to select the participants during a visit to the HIV/AIDS care unit for counseling and/or ART medication. The sample size was 86 HIV-infected.

Data collection

A face-to-face interview with PLHIV by trained interviewers at the HIV/AIDS center was conducted using a structured, self-report questionnaire developed by the Adult AIDS Clinical Trials Group (AACTG)[17] and slightly modified after a pre-testing at the PHC. The AACTG was developed based on previous adherence to medical regimen research and has been extensively used to measure ART adherence. This consisted of a standardized questionnaire and face-to-face exit interviews with participants. The questionnaire had been initially tested for validity and reliability. Validity was established by a panel of experts and following a field test that determined whether the questionnaire measured what it intended to measure, whether it represented the appropriate content, whether it was appropriate for the study population and whether it was comprehensive enough to collect the needed information. Reliability was computed after a pilot field test to indicate the accuracy of the measuring questionnaire using test-retest approach. The questionnaire was divided into sections to collect relevant information on: socio-demographic data, information regarding: WHO staging, ARV regimen, total number of other tablets, total number of ARV tablets, initial $CD4^+$ T-cell count, current $CD4^+$ T – cell count, and time on ART. Other information collected were: psychosocial/behavioral characteristics, patient attitudes and beliefs, social relationships/activities, medication characteristics, patient knowledge on the medicines, health-care practitioner-patient communication, pill count, times taken in different places (minutes, hours). Adherence to HAART of the interview was measured by self-report.

The adherence rate from pill-count was calculated using the following formula[18]: Percentage of adherence (%) = (Tablets dispensed – Tablets returned) / expected to be taken x100. For the purpose of this study a score of 95% and above represented good adherence and less than 95% was rated as having poor/suboptimal adherence. The questionnaire asked patients to recall their medication intake in terms of their prescribed doses for the three days prior to the interview. The questionnaire also contained questions on seriousness of the disease, side effects and adverse drug reactions. In addition, there were also questions about health service-related characteristics of the center providing ART. Prior to administration, the questionnaire was translated into the local language (IsiXhosa) and English and back translated by an independent translator. To ensure confidentiality, all respondents were interviewed in a private room at the HIV/AIDS care unit by the trained interviewers.

Measurement of adherence

Adherence measurement in this study was based on patient recall of their compliance of the prescribed doses in the three days prior to the interview. Adherence was calculated based on the number of pills reported to have been actually taken divided by the number of prescribed pills over in the one month. Patients who after the calculated adherence rate had an intake of ≥95% of the prescribed medication were considered adherent, those with an intake of < 95% were classified as non-adherent.

Data analysis

Data were coded and captured in the computer using MS Excel® and analyzed using SPSS® for windows version 22.0 (SPSS Inc; Chicago, Il, USA). Descriptive and inferential statistical tests were employed. These included univariate (chi-square) and multivariate (logistic regression) analysis to determine correlates or predictors of adherence. Descriptive statistics (frequencies, proportions, means and standard deviation to summarize variables while Inferential statistics (chi square Test) was used to test the significance of association between categorical variables and level of significance was set at 5%. Logistic regression analysis was then used to identify the predictors of adherence to HAART in the study population. Predictors were determined at 5% significance. Factors associated with poor adherence to HAART were accessed with ANOVA and; a $\rho \leq 0.05$ was considered statistically significant.

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Ethical considerations
Ethical clearance was obtained from the Walter Sisulu University, Faculty of Health Sciences and Research Innovation and Ethics Committees. Ethical Clearance issued was 015/012. Thereafter permission to conduct the study was sought from the department of health and the manager of the municipality where the PHC is located, thereafter permission to conduct the interviews to the patients were obtained from the relevant clinic manager or supervisor. Before the interviews, patients were explained the aim of the study and procedures using the Patient Information sheet and thereafter asked to sign a written informed consent form which was optional. To maintain confidentiality of the patients no names of patients appeared on the forms. The participants were also informed that their participation was voluntary and that they could withdraw from the interview/ discussion at any time without consequences.

The participants were assured that their responses would be treated in confidence and they were assured anonymity through the use of strict coding measures

Results
Socio-demographics
Gender distribution (n=86)
Of the 86 recruited patients, of these 63 (73.3%) were females and 23 (26.7%) males with mean age (±SD) of 35.6 (±9.6) years and were enrolled on HAART for 35.5 (±31.8) months. As seen in Table 1, of the 32 (37.2%) patients that were computed, 25 (29.1%) were females and 18 (20.9%) males. Of these 7 (77.8%) females were reported adherent as opposed to 2 (22.2%) males adherent. There was no univariate association between age of patients and adherence rate ($p = 0.56$).

Age in years (patients)
The patients interviewed the age range of patients was from < 34 to ≥ 45 years old. This is the key age group of adults that represented the majority of patients. Of these those below 34 years 44.4% were adherent, while 39.1% were not adherent to ARV treatment. This shows that there are higher HIV infection rates among young and working class women especially those aged between 20 and 49 years compared to young men. There was no univariate association between age of the patients and adherence rate for $p = 0.56$.

Marital status
As demonstrated in Table 1, the majority of respondents 21(24.4%) were singles, while 8(9.30) were married. Of the singles, 66.7% were adherent as compared to 65.2 that were non-adherent. Whereas among the married ones 33.3% were adherent, 21.7% were non-adherent.

There was no univariate association between marital status of the patients and adherence rate for $p = 0.66$.

Educational level
As depicted in the table, all higher number of respondents 25 (29.86%) had secondary level of education. Of these, 7 (87.5%) had acceptable adherence rate, while 4 (17.4%) had poor adherence rate. There was no univariate association between educational level and adherence rate for $p = 0.36$.

Employment status
Figure 1 depicts that about 21 (24.4%), of all patients that were interviewed showed that they were unemployed while 10 (11.63%) were unemployed. Of the unemployed patients 6 (66.7%) were adherent while 15 68.2%) were non-adherent. Those that were employed 5 (5.81%) earned a salary of R 2000-4000 per month. Findings from this study showed that there was no association between employment status and adherence rate with a $p = 0.63$.

Salary earned
Of the patients that were interviewed, the majority earned between R 2000-4000 per month with all 4 (57.1%) that earned less than R2000 being non adherent and only 1(33.3%) who earned R4000 having acceptable adherence rate. The was a univariate association between the amount of money earned per month and adherence rate giving a p value of 0.043.

Adherence level
Eighty six HIV-infected patients were recruited for this study, of these 63 (73.3%) were females and 23 (26.7%) males with mean age (±SD) of 35.6 (±9.6) years and were enrolled on HAART for 35.5 (±31.8) months. Of the 32 patients that were computed, 25 (29.1%) were females and 18 (20.9%) males. Of these 7 (77.8%) were reported adherent as opposed to 2 (22.2%) males adherent.

Only eight participants were married of which 33.3% were adherent while 21.7% non-adherent. Majority of the respondents (78.1%) had obtained secondary school certificates. Once again the majorities of respondents (65.6%) were unemployed and received a monthly income of ≤ 2000 South African Rands (see Table 1).

Health Risk behavior characteristics
Time on ART
The respondents had been enrolled on HAART for 35.5 (±31.8) months ranging from 1–137 months with mean age (±SD) of 35.6 (±9.6) years. The majority of patients 14 (16.3%) had been on ART for a period of 12-36 months and of these 3(33.3) were adherent to their treatment while 11(47.8%) were not. There was no univariate association between time on ART and adherence rate for $p = 0.76$ which was none significant.

WHO staging
The majority of the patients 14 (16.3%) were classified in the HIV stage 3 based on WHO staging. All 14 (63.6%) patients in WHO stage 3 were none complaint. There was an association between WHO-staging 2 and 3 and adherent rate that was statistically significant ($\chi 2=12.09$, $p = 0.007$).

Initial and Current CD4 T-cell count
The majority of patients 15 (17.44%) had initial CD4-count of less than 200 cell/uL, with 6 (66.7%) adherent and 9 (50%) non-adherent. These patients had severe immune suppression with recorded CD4 T–cell lower than 200 cells/uL, while 7 (8.1%) had CD4 T-cell counts of 200-349 cells/uL. Patients with the current CD4 T-cell count had values of ≥500 cells/uL and all were non-adherent. The mean CD4 T-cell count at the initiation of HAART was 232.4 (±169.2) cells/mm^3, the latest was 433.7 (±242.9) cells/mm^3 with most respondents (46.9%) having CD_4 cell counts of less than 350 mm^3 which was the threshold to ART treatment according the South African National Treatment Guidelines (19). Despite an observed overall improvement of patients' immune response following HAART in terms of CD4 cell-count, there was no association between Initial and current CD4 cell-counts with adherence rates with $p = 0.55$ and $p = 0.40$ respectively.

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ARV regimens
Of 86 HIV-infected patients, 73.3% were females and 26.7% males with mean age (±SD) of 35.6 (±9.6) years and were enrolled on HAART for 35.5 (±31.8) months. Adherence-rate was computed from 32 patients and revealed that 71.9% having poor adherence-rate.

Of the computed 32 patients, the majority of the patients 24 (75%) were on regimen that contained lamivudine, tenofovir and Efavirenz (1A-TDF), followed by those 9 (28.1%) that were on fixed dose combination (FDC): Emtricitabine, tenofovir and efavirenz. Thirty-two (37.2%) patients on Lamivudine (3TC), Tenofovir (TDF) and Efavirenz (EFV) (regimen 1A-TDF) 24 (75%) had poor adherence-rate. Patients on regimens 1A-TDF and TDF reported of experiencing adverse effects relating to CNS (35.3%) followed by 23.3% related to ENT side effects. There was no univariate association of statisticall significance between ARV regimens and adherence rates with p = 0.78.

Total number of ARV tablets
Of the participants 10 (11.6%) received 4 ARVs tablets and of these, 9 (40.9%) were none adherent while only one was adherent. There was no univariate association between number of ARVs and adherence rate giving p of 0.31. However patients who received other tablets other than ARVs (≥4 combined tablets) had univariate association with adherence rate ($\chi 2$ =10.81, p =0.029).

Discussion
Comparing socio-demographic characteristics and adherence rates, the results in this study revealed that there were more females than males that are living with HIV and that females were more adherent than males as seen in Table 1. This confirms the inequalities between men and women that are created and reinforced by gender roles, typically leaving women especially vulnerable to HIV infection. According to Van Dyk,[18] women are more likely than men to become infected with HIV during unprotected vaginal intercourse. There are various biological, cultural, and social reasons which make women more susceptible to HIV infection than men. As the recipients of semen, they are exposed to semen for a longer time. They also have a larger surface area of mucosa (the thin lining of the vagina and cervix) exposed to the partner's secretions during sexual intercourse.

Apart from their biological vulnerability, women become more vulnerable in societies in which they are seen as having lower status than men, which makes them dangerously vulnerable in sexual relationships.[18] The findings of this study are also supported by EL-Khatib et al.[19] in previous studies in South Africa and also confirmed by Statistics SA,[20] that that in South Africa, just over 51% (27.08 million) of the population are females and the ratio of new female infections to male for those aged 15 to 49 was 1.5 by 2013. This was further confirmed by recent data from 2015 Statistics SA [21] estimating 54.96 million mid-year population and approx 51% (28.07 million) of population being female. Overall HIV prevalence rate was 11.2% of total population with total no of PLHIV estimated at 6.19 million and of these, 80% of 20-24 yrs of HIV infected are women.

One study by Potchoo et al.[22] in Togo and another study by Talam et al.[23] in Kenya, both performed among HIV adult patients in clinic settings also had higher proportions of female respondents as compared to males.

Age in years (patients)
Results from this study indicated that age group > 34 years presented most infected HIV-patients. And of these 44.4% were more adherent as opposed to 39.1% and among these 7(77.8%) were females and 2(22.2) males. This shows that there are higher HIV infection rates among the young and working class women especially those aged between 20 and 49 years compared to young men. According to UNAIDS,[24] in 2013, the total no of PLHIV was estimated at 6.19 million and of these, 80% of 20-24 years of HIV infected were women.

The finding of this study correlate with the evidence from studies performed by Mutinta et al.[25] in South Africa which showed that some gender norms related to masculinity encourage men to have more sexual partners and older men to have sexual relations with much younger women. In addition, this contributes to higher HIV infection rates among young and working class women, especially those aged between 15 and 49 years compared to young men.

Marital status
Results from this study revealed a greater number of HIV infected being singles as compared to the married ones. This shows that in relation to the marital status and HIV infection, being single amplifies the risk of getting infected with HIV because these individuals are likely to be engaged in many risk-taking behaviors including casual sex, multiple and concurrent sexual partnership and failure to use condoms during sex. This finding agrees with a study[26] done in Zimbabwe in 2014, which found that being single was associated with HIV infection (Ministry of Health and Child Care, 2014). In addition, Shisana et al.[27] in their study in found that in South Africa HIV infection varied considerably by marital status. Those that are married are less likely to be HIV positive compared to any other reported marital status.

Educational level.
Participants that had secondary level of education presented most at the clinics with 25 (29.1%). A study performed by Afolabi et al.[28] in Nigeria by bivariate analyses showed that higher education was significantly associated with good knowledge about ART, and therefore higher adherent rates. Despite no association between educational-level and adherence-rate (p=0.36), all pts with primary- level of education were non-compliant with adherence rate of 17.4%.

Employment Status
Figure 1 depicts that about 21 (24.4%) of all patients that were interviewed showed that they were unemployed while 10 (11.63%) were employed. Of the unemployed patients 6 (66.7%) were adherent while 15 68.2%) were non-adherent. Those that were employed 5 (5.81%) earn R 2000-4000 per month. This finding suggests that the socio-demographic context in which people live highly influences the individual risk of exposure to HIV-infection. In addition, this finding agrees with a study done by Blattman[29] in 2011 which found that being HIV positive is associated with increase in the likelihood of being unemployed. McLaren[30] in 2011in his study, found that in South Africa, individuals with HIV tend to be unemployed, and unemployed people are more likely to be HIV positive. Furthermore, Levinsohn et al.[31] in 2011, found that being HIV-positive is associated with a 6 to 7% point increase in the likelihood of being unemployed.

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Adherence level

According to literature, antiretroviral therapy reduces the HIV viral load as much as possible, preferably to undetectable levels for as long as possible. In this study there were no records of initial and recent viral loads. But for the CD4 T cell count as observed in the table of results, the mean CD4 T cell count at the initiation of HAART was 232.4 (±169.2) cells/mm^3, the latest was 433.7 (±242.9) cells/mm^3 with most respondents (46.9%) having CD_4 cell counts of less than 350 mm^3 which was the threshold to ART treatment according the South African National Treatment Guidelines. There was observed overall improvement of patients' immune response following HAART in terms of CD4 cell-count. With HAART, the CD4 T-cell lymphocyte count usually increases progressively. Although there were patients that still had severe immune suppression with CD4 T cell count less than 200 cells/uL. Typically, the CD4 count increases rapidly by approximately 50 to 100 cells/mm3/year.[18, 32]

In addition, CD4 responses are highly variable and may fail to increase despite virological suppression and a small proportion of patients who start antiretroviral therapy with a very high viral load may not be fully suppressed despite being adherent to the treatment.[32-33]

One possibility for the findings from this study could suggest that patients may not take all dispensed medications or another possibility could be that they take them in not prescribed amounts or off the prescribed schedules, or fail to match the dose with food as directed. One could also argue that patients could share or even sell their own ARVs to avoid discrimination and stigma in community or family.

According to Zaragoza-Macias et al.[34] in their study performed in 2012, it was revealed that the relationship between refills and actual ingestion of medications is not clear and it is therefore difficult to measure adherence in the outpatient setting accurately and correctly. Other literature state that ART reduces the HIV viral load as much as possible, preferably to undetectable levels for as long as possible. By doing so, the CD4 T-cell lymphocyte count usually increases progressively. According to Van Dyk,[18] in 2013 and Meintjes et al. [32] in 2012, typically, the CD4 count increases rapidly by approximately 50 to 100 cells/mm3/year. In addition, CD4 responses are highly variable and may fail to increase despite virological suppression and a small proportion of patients who start antiretroviral therapy with a very high viral load may not be fully suppressed despite being adherent to the treatment.[32-33]

ARV regimens

Of 86 HIV-infected patients, 73.3% were females and 26.7% males with mean age (±SD) of 35.6 (±9.6) years and were enrolled on HAART for 35.5 (±31.8) months. Adherence-rate was computed from 32 patients and revealed that 71.9% having poor adherence-rate.

Thirty-two (37.2%) patients on Lamivudine (3TC), Tenofovir (TDF) and Efavirenz (EFV) (regimen 1A-TDF) 24 (75%) had poor adherence-rate. The commonest adverse effects (ADEs) experienced by patients on regimen 1A-TDF and TDF, Emtricitabine (FTC) and EFV (regimen FDC) were CNS-related (35.3%) followed by ENT (23.3%). Evaluated variables associated with poor-adherence to HAART were: salary ≥ R2000 (χ2=4.3,p=0.043); WHO-staging 2 and 3 (χ2=12.09,p=0.007) and total number of other tablets (≥4 combined tablets) (χ2 =10.81,p=0.029).

It is important for healthcare providers to consider crucial factors that are related to patients initiating ART. These include compliance to regular clinic visits, counseling, availability of support services and a multidisciplinary approach. Patients should receive a complete understanding of the complexity of the regimen, side effects and scheduling, among other concerns, may help patients deal with their medication with less difficulty. In addition, earlier access to care and counseling before actual ART may help prepare patients for long-term treatment effects and reinforce the need for high adherence.

Patients in this study that were on regimens containing Efavirenz were non compliant because they complained of CNS-related adverse effects. Clinical- and treatment-related factors were found to be barriers for good adherence. Adverse effects indicated a stronger early effect of treatment and were commonly cited as the main reason for difficulty with patients not continuing with their treatment.

Results from this study are consistent with the results obtained in the studies by Bonolo et al.[35] in 2005 in Brazil, Eriksson at al.[36] in 2005, Abel & Painter,[37] in 2003 and Ammassari et al.[38] in 2001 indicated that adverse effects are related to a decrease in the quality of life and low adherence among HIV-treated patients. However, ART is a dynamic phenomenon, which changes over time, as stated by Remian et al. [39] in a study performed in USA in 2003, that patients tend to adapt their daily routine to regimen scheduling and more readily learn how to identify and deal with side effects.

However, pill burden, the inclusion of regimens with protease inhibitor and the additional use of other medications over time are factors which also tend to create more difficulties as was demonstrated in this study. There was a univariate association between the total number of other tablets and adherence rate with a p = 0.029 that was statistically significant.

Additionally, it should be noted that even if patients are adequately counseled when beginning treatment, long-lasting and sustained good levels of information may not be feasible if routine counseling and reminders by health professionals are not continuously received by patients. Finally, the association of a higher CD4+ cell count and the asymptomatic patient designation (CDC classification A) with increased difficulties may reflect a lower perception of these patients with regard to the need for treatment, and thus a lower threshold for dealing with the daily burden of ART regimens.

Limitations from the study

The viral loads were not captured from the patients' record due not being entered regularly.

Conclusion

Despite an observed overall improvement of patients' immune response following HAART, poor- adherence remains a major challenge due to: ADEs associated with regimen 1A-TDF, FDC, the burden associated with the use of ≥4 combined tablets, clinical improvement, and lower earnings**.** Evaluated variables associated with poor-adherence to HAART were: salary ≥ R2000 (χ2=4.3, p=0.043); WHO-staging 2 and 3 (χ2=12.09, p=0.007) and total number of other tablets (≥4 combined tablets) (χ2 =10.81, p=0.029).

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Table 1: Univariate associations between determinants of interest and poor adherence to HAART in HIV-infected (N = 86)

Factors of interest	Acceptable adherence rate ≥ 95% N (%)	Poor adherence rate ≤ 95% N (%)	P - value
Age (years)			0.56
< 34	4 (44.4)	9 (39.1)	
35 – 44	3 (33.3)	8 (34.8)	
≥ 45	(22.2)	6 (26.1)	
Gender			0.66
Female	7 (77.8)	18 (78.3	
Male	2 (22.2)	16 (21.7)	
Marital Status			0.68
Married	3 (33.3)	5 (21.7)	
Single	6 (66.7)	15 (65.2)	
Divorced	0 (00.0)	1 (4.3)	
Separated	0 (00.0)	2 (8.7)	
Educational Level			0.36
Primary	0 (0.0)	4 (17.4)	
Secondary	7 (87.5)	18 (78.3)	
Tertiary	1 (12.5)	1 (4.3)	

Table (cont): Univariate associations between determinants of interest and poor adherence to HAART in HIV-infected (N = 86)

Factors of interest	Acceptable adherence rate ≥ 95% N (%)	Poor adherence rate ≤ 95% N (%)	P - value
Employment Status			0.63
Employed	3 (3.33)	7 (31.8)	
Unemployed	6 (66.7)	15 (68.2)	
Salary (Rands)			0.043
<2000	0 (0.0)	4 (57.1)	
2000 – 4000	2 (66.7)	3 (42.9)	
>4000	1 (33.3)	0 (0.0)	
WHO Stage			0.007
1	3 (60.0)	1 (4.5)	
2	1 (20.0)	5 (22.7)	
3	0 (0.0)	14 (63.6)	
4	1 (20.0)	2 (9.1)	
ARV Regimen			0.78
1A	0 (0)	1 (4.3)	
1A TDF	12 (52.2)	12 (52.2)	
1B	3 (13.0)	3 (13.0)	
1B TDF	0 (0)	1 (4.3)	
NON STANDARD	0 (0)	1 (4.3)	
FDC	4 (44.4)	5 (21.7)	

1A = Lamivudine, Stavudine, Efavirenz; 1A TDF = 3TC, Tenofovir, EFV; 1B = 3TC, D4T, NVP; 1B TDF = 3TC, TDF, NVP; NON- STANDARD = Aluvia, 3TC, TDF; FDC = Emtricitabine, EFV, TDF

Table (cont): Univariate associations between determinants of interest and poor adherence to HAART in HIV-infected (N = 86)

Factors of interest	Acceptable adherence rate ≥ 95%	Poor adherence rate ≤ 95%	P-value
Current CD4⁺ T – cell count (cells/uL)	N (%)	N (%)	0.40
<200	1 (25.0)	2 (15.4)	
200 – 349	1 (25.0)	2 (15.4)	
350 – 499	2 (50.0)	3(23.1)	
≥500	0(0.0)	6 (46.2)	
Time on ART			0.76
< 12 months	3 (33.3)	6 (26.1)	
12 – 36 months	3 (33.3)	11 (47.8)	
> 36 months	3 (33.3)	6 (26.1)	

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Table (cont): Univariate associations between determinants of interest and poor adherence to HAART in HIV-infected (N = 86)

Factors of interest	Acceptable adherence rate ≥ 95%	Poor adherence rate ≤ 95%	P-value
Total Number of other tablets	**N (%)**	**N (%)**	**0.029**
1	3 (33.3)	2 (8.7)	
3	2 (22.2)	14 (60.9)	
4	0 (0.0)	5 (21.7)	
5	2 (22.2)	1 (4.3)	
6	2 (22.2)	1 (4.3)	
Number of ARVs tablets			**0.31**
1	3 (33.3)	3 (13.6)	
2	0 (0.0)	1 (4.5)	
3	2 (22.2)	5 (22.7)	
4	1 (11.1)	9 (40.9)	
5	2 (22.2)	4 (18.2)	
6	1 (11.1)	0 (0.0)	
Initial $CD4^+$ T – cell count (cells/uL)			**0.55**
<200	6 (66.7)	9 (50.0)	
200-349	2 (22.2)	5 (27.8)	
350 – 499	0 (0.0)	3 (16.7)	
≥500	1 (11.1)	1 (5.6)	

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