

*Full Length Research paper*

# Prevalence and determinants of non-adherence to antiretroviral therapy among HIV- positive pregnant women in Nnewi, Nigeria

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Adherence to antiretroviral therapy (ART) is central to a successful prevention of mother- to- child transmission of HIV (PMTCT) programme by ensuring optimal viral suppression. However, barriers to adherence exist and differ among populations. This cross-sectional study was carried out among 368 HIV-positive pregnant mothers attending the PMTCT clinic at Nnamdi Azikiwe University Teaching Hospital Nnewi, Nigeria to determine the prevalence and demographic variables related to non-adherence to ART. The mean age and parity of the women were  $30.4 \pm 4.4$  years and  $2.5 \pm 2.0$  respectively. Majority (97.0%) were married and had achieved secondary education and above (86.9%). One hundred and sixty five (44.8%) had been on ART for more than 2 years while 37.0 % commenced ART in the index pregnancy. The non adherence rate was 21.7%. The common reasons for missing ARV drugs were forgetfulness (63.8%); feeling healthy and hence no need to take ARV drugs (16.3%) and living very far from the hospital (15.0%). Increasing maternal age ( $X^2 = 13.6$ ;  $P = 0.001$ ), low educational level ( $X^2 = 39.36$   $P = 0.002$ ), extremes of parity ( $X^2 = 11.3$   $P = 0.03$ ), husband's low educational level ( $X^2 = 13.8$ ;  $P = 0.01$ ), being in a sero-concordant relationship ( $X^2 = 6.2$ ;  $P = 0.05$ ) and non-disclosure of HIV serostatus ( $X^2 = 12.96$ ;  $P = 0.003$ ) were significantly associated with non adherence to ART. Those women who had been on ART for up to 2 years and beyond ( $X^2 = 9.52$ ;  $P = 0.001$ ), and those in whom the diagnosis of HIV was made before pregnancy ( $X^2 = 5.21$ ;  $P = 0.02$ ) were more likely to be non-adherent to therapy. These factors are recommended to guide counseling and design of programmes aimed at reducing non-adherence to ART.

**Key words:** Non-adherence, anti retroviral therapy, PMTCT, Nnewi, Nigeria.

## INTRODUCTION

The rate of mother to child transmission of HIV infection as well as the survival of people diagnosed with HIV/AIDS dramatically improves with access to highly active antiretroviral therapy (HAART). HAART consists of three or more antiretroviral agents to be taken in combination and is the standard of care for prevention of mother to child transmission of HIV (PMTCT). Such therapy employs a combination of protease inhibitors (PIs), nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs/NtRTIs), non-nucleoside reverse transcriptase inhibitors, and fusion inhibitors etc, to suppress

viral replication (Mannheimer et al., 2006; Tadios and Davey, 2006; WHO, 2003). The therapy involves the ingestion of many pills twice or thrice daily. This enormous pill burden associated with HAART is a major challenge in HIV management and PMTCT programmes. In addition some antiretroviral agents also require specific food and fluid restrictions. Furthermore, HAART has some side effects that may be temporary such as nausea, vomiting, diarrhoea, fatigue, or long-lasting conditions such as neuropathy, lipoatrophy/lipodystrophy, and metabolic dysfunction. These side effects have been shown to be contributory to non-adherence to ART (Monreal et al., 2002).

The goal of HAART in PMTCT is to achieve maximal viral suppression so as to reduce vertical transmission and

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to provide prophylaxis for the baby. In addition, HAART reduces immune suppression, slows disease progression and improves patients' quality of life (Mannheimer et al., 2006). Success of HAART is evidenced by rising CD4 cell counts, undetectable viral loads, clinical improvement in patients and ultimately, reduced MTCT rate. As viral load assays are expensive in PMTCT programmes in resource-limited settings, CD4 counts and Clinical status are the main tools for monitoring treatment outcomes.

Poor compliance with and non-adherence to HAART leads to the exposure of the virus to inadequate concentrations of antiretroviral medications. This in turn leads to ongoing viral replication, development of resistance to antiretroviral medications and increased vertical transmission. There is also the critical problem of 'cross-resistance'. Once the virus becomes resistant to a particular antiretroviral drug, it may also exhibit resistance to other medications in the same class that have not yet been prescribed to that patient.

This limits the choice of drugs available to replace failing regimen. For example, resistance to Nevirapine would mean that the patient cannot use other NNRTI medications such as Delavirdine or Efavirenz. There is increasing evidence that drug resistance is highest among those taking mainly regimens containing a non boosted PI (that is, regimens without ritonavir), among those with intermittent or single-dose regimens of non-nucleoside reverse transcriptase inhibitors, and among people with poor adherence to antiretroviral drugs (Bangsberg et al., 1999; Yerly et al., 2007; Kozal, 2009).

The second issue with viral resistance is its transmission. It has been reported that some patients diagnosed for the first time with HIV, who have never taken ARVs, are already resistant to some anti-retroviral medications (Little et al., 2002). This is a major public health problem in resource-limited situations where the choice of medications is already restricted due to high costs and limited availability.

Therefore, measures to ensure adherence to antiretroviral therapy has been a key component of many programmes to reduce the risk of HIV transmission. Within the context of PMTCT particularly, optimal viral suppression is desired to reduce the rate of vertical transmission of HIV infection.

Adherence is defined as 'the act or quality of sticking to something'. In the context of treatment with medications, adherence means a more collaborative process between the patient and health-care provider. The patient plays a more active role in his treatment and makes a commitment to follow the prescribed regimen as best as possible as different from "compliance" which means the act of conforming, yielding or acquiescing to treatment without the patient's active participation. Adherence to treatment is critical to obtaining the full benefits of HAART, maximal and durable suppression of viral replication, reduced destruction of CD4 cells, prevention of viral resistance, promotion of immune reconstitution, slowing progression of disease and reducing MTCT rates (Nachega et al., 2006;

Bangsberg et al., 2001).

The level of adherence that guarantees optimal viral suppression is still controversial. However, Paterson et al. (2000) found that in order to achieve this degree of viral load suppression, a person on HAART needs to take at least 95% of the prescribed doses on time. For many people, this means taking a regimen of three antiretroviral agents at the same time twice daily, which usually involves taking several pills (Partners in Health, 2004).

There are many ways of assessing clients' adherence to ARVs but generally it is difficult to measure adherence in the outpatient setting with absolute precision and accuracy (Flexner, 1997). While there may be no gold-standard with which to measure adherence, available methods include, self-reports (including surveys, interviews and diaries), clinical assessments, pill counts, directly observed therapy (DOT), prescription refills, biological markers, therapeutic drug monitoring (TDM) and medication event monitoring system (MEMS) (Besch, 1995; Bonds and Hussar, 1991; Cramer et al., 1998).

Studies on adherence use one or more of these tools but most of these studies have used the self reported adherence method which have been shown to correlate very well with viral load and CD4 count tests (Sethi et al., 2003; Spire et al., 2002; Chesney et al., 2000). However estimations by health-care providers may lead to inaccurate results (Moatti et al., 2004).

Adherence to ART is pivotal in reducing MTCT, preventing the emergence of drug resistant strains, and improving life expectancy of people with HIV infection. Therefore, barriers to adherence should be given a priority attention when allocating resources and designing programmes to control HIV infection in resource poor countries where the HIV infection abound. Some authors have argued that the barriers to adherence are insurmountable in resource-poor settings, so there should be caution in delivering ART to these populations. However adherence in resource-poor settings has been shown to be similar to that in developed countries (Coetzee et al., 2004; Katzenstein et al., 2003; Koenig et al., 2004; Laniece et al., 2003; Olowookere et al., 2008).

Although some studies have been carried out on the rate and determinants of non adherence to antiretroviral therapy among HIV-positive clients in Nigeria (Olowookere et al., 2008; Shaahu et al., 2008; Iliyasu et al., 2005), they were mostly done among the non pregnant population. The aim of this study was to determine the level and identify factors associated with non adherence to ARVs among HIV-positive pregnant women in our environment. The knowledge shall be useful in designing effective strategies to improve their level of adherence and ultimately minimize the mother to child transmission of HIV.

#### STUDY DESIGN/SETTING

This is a cross sectional study carried out over six months (September 2009– February 2010) at the PMTCT clinic of Nnamdi

**Table 1.** Socio-demographic - profile of HIV-positive pregnant mothers on HAART at PMTCT clinic, Nnamdi Azikiwe University Teaching Hospital, Nnewi Nigeria.

Socio-demographic factor	Frequency	(%)
<b>Age (years)</b>		
20-29	175	47.8
30-39	169	45.7
40 and above	24	6.5
<b>Parity</b>		
0-1	120	32.6
2-4	200	54.3
5 and above	48	13.1
<b>Marital status</b>		
Married	337	91.6
Single	25	6.8
Widow	6	1.6
<b>Educational status</b>		
No formal	8	2.2
Primary	40	10.9
Secondary	264	71.7
Tertiary	56	15.2
<b>Religion</b>		
Catholic	159	43.5
Pentecostal	113	30.4
Anglican	96	26.1
<b>Occupation</b>		
Trading	208	56.5
Housewife	64	17.4
Public servant	56	15.2
Artisan	24	6.5
Student	16	4.4

Azikiwe University Teaching Hospital, Nnewi, Nigeria which is one of the upgraded sites for PMTCT programme in the country.

#### Sample size

The minimum sample size was determined by using the statistical formula of Fisher for calculating sample size (Araoye, 2003).

$$N = Z^2 pq / d^2$$

Where: N = Minimum sample size for a statistically significant survey; Z = Normal deviant at the portion of 95% Confidence interval = 1.96; P = Prevalence value of non-adherence in a health facility = 37.1% (Olowookere et al., 2008); q = 1 - p; d = Margin of error acceptable or measure of precision = 0.05; N = 358; Minimum sample size = 358.

The sample size was adjusted by 3%

Therefore, sample size = 368.

#### SUBJECTS AND METHODS

Three hundred and sixty eight consecutive HIV positive pregnant women attending PMTCT clinic at the Nnamdi Azikiwe University Teaching Hospital, Nnewi who gave their consent for the study were recruited. They were interviewed as they attended the clinic. All the women had been on ARVs for at least three months preceding the study. With the aid of pre-tested, semi structured questionnaires, information on biosocial characteristics were obtained, and adherence to antiretroviral therapy was assessed using the self-report method.

They were interviewed on the number of pills missed in the preceding one month and adherence was defined as having taken at least 95% of the totally prescribed pills at the prescribed dosing intervals. For instance, for a respondent on nevirapine which is taken twice a day, one should take 60 pills over one month (30 days). To achieve 95% adherence, the patient must take at least 57 of these 60 tablets at the same time daily. Missing more than three pills or doses would result in less than 95% adherence (Paterson et al., 2000). Women who withheld consent, who were mentally subnormal, and who had not been on therapy for up to 3 months were excluded from the study.

Data analysis was done with Epi info statistical package, version 3.5.1. Student's t-test was used to compare means, while Chi square tables (Yates corrected and 2-tailed Fisher exact test) were used to determine the effect of demographic factors and other variables on the likelihood of non-adherence to ART. A p-value of  $\leq 0.05$  at 95% confidence interval was taken as statistically significant. The data is presented in tables and a chart.

#### RESULTS

Three hundred and sixty eight HIV-positive pregnant mothers were interviewed. Eighty mothers were non-adherent to HAART giving the non adherence rate of 21.7%.

Table 1 shows the socio-demographic profile of the respondents. The mean age of the respondents was  $30.4 \pm 4.4$  SD years. The modal parity group was 2 - 4 (54.3%) while the mean parity was  $2.5 \pm 2.0$ SD. Majority (91.6%) of the respondents were married and most of them were traders (56.5%) and had achieved secondary school education and above (86.9%). There was no statistical difference between the mean age of the adherents and non adherents (t-test = 0.53; p = 0.50).

Table 2 shows other characteristics of the respondents. Three hundred and twenty five (88.3%) had disclosed their HIV status to their partners and 91.3% knew their husband's HIV-status, among whom 41.3% were HIV-negative. One hundred and sixty five (44.8%) had been on ARV drugs for more than 2 years while 38.0 % commenced ARV drugs in their index pregnancy.

Table 3 shows the influence of socio-demographic factors and other variables on non-adherence. Pregnant mothers aged 40 years and above ( $X^2 = 13.61$ ; P = 0.001), low educational level ( $X^2 = 39.36$  P = 0.002), extremes of parity ( $X^2 = 11.32$  P = 0.03), husband's low educational level ( $X^2 = 13.75$ ; P = 0.01), being in a

**Table 2.** Other characteristics of HIV-positive pregnant mothers on HAART at PMTCT clinic, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria.

Characteristics	Frequency	(%)
<b>Disclosure of HIV-status partner</b>		
Yes	325	88.3
No	43	11.7
<b>Duration of ARVs</b>		
< 2yrs	63	17.1
2 - 5yrs	161	43.7
5 - 10 yrs	4	1.1
In the index pregnancy	140	38.0
<b>Partners' HIV-status</b>		
Positive	184	50.0
Negative	152	41.3
Unknown	32	8.7

sero-concordant relationship ( $X^2 = 6.2$ ;  $P = 0.05$ ) and non-disclosure of HIV serostatus ( $X^2 = 12.96$ ;  $P = 0.003$ ) were significantly associated with non adherence to ART. Women who were artisans and full time house wives were more likely to be non-adherent ( $X^2 = 64.02$ ;  $P = 0.001$ ). All the 16 students were adherent to ART. In addition, those who had been on ART for up to 2 years and beyond ( $X^2 = 9.52$ ;  $P = 0.001$ ), and those in whom the diagnosis of HIV was made before pregnancy ( $X^2 = 5.21$ ;  $P = 0.02$ ) were more likely to be non-adherent to therapy. There was no significant association between marital status and adherence to ART.

Figure 1 show the reasons for non adherence among the 80 respondents who were non-adherent. The reasons given for missing drugs were forgetfulness 51(63.8%); feeling healthy and hence no need to take drugs 13 (16.2%), and living very far from the hospital 12 (15.0%). Four (5.0%) women were non-adherent on account of the side effects of the drugs.

## DISCUSSION

This study recorded a non adherence rate of 21.7% among HIV-positive pregnant women. This is slightly higher than 16.3% ( $n = 69$ ) reported in Zambia (Carlucci et al., 2008), but lower than 37.1 % ( $n = 118$ ) and 37.4% ( $n = 160$ ) reported by Oloowokere et al. (2008) and Shaahu et al. (2008), respectively in Ibadan, Southwestern Nigeria. The association between non-adherence to ART and virologic and clinical failures is well documented (Sethi et al., 2003; Spire et al., 2002; Chesney et al., 2000; Low-Beer et al., 2000; Gifford et al., 2000; Haubrich et al., 1999; Robbins et al., 2007). Therefore for this 21.7% of the pregnant women enrolled

in the PMTCT programme, the risk of virologic failure and the chances of vertical transmission are high. This is in spite of the fact that all the women had adherence counseling prior to the initiation of ART. This may indicate a need to review pre commencement adherence counseling practice in the area in terms of organization, content and delivery. It may be important to survey the knowledge of the trained counselors and possibly organize periodic re-training. Proper evaluation of the clients for beliefs and attitudes is central to effective counseling as studies have shown that clarification of clients' beliefs and attitudes during adherence counseling significantly improve their level of adherence to ART (White et al., 2006).

As antiretroviral therapy in pregnancy is not solely for preventing/controlling maternal disease, there is the need to emphasize the basis of the therapy and possibly back it up with evidence. From this study, a significant number of the non-adherents missed their drugs because they felt healthy and hence, no need for the drugs. This also suggests a need to further impress on the women that the antiretroviral drugs are not meant for their own health conditions but to prevent infecting their unborn babies with HIV.

The main reason given for missing drug was forgetfulness. Similar findings were documented in Ibadan, Nigeria (Oloowokere et al., 2008) and Ethiopia (Amberbir et al., 2008). Other reasons noted in the Ethiopian study include feeling sick, being busy and running out of medication. Although we didn't evaluate these factors, running out of stock is not likely a reason for our women as the drugs are provided free of charge.

Measures that have been utilized to reduce the tendency of patients on ART to forget taking their drugs include the use of electronic reminder devices (Wise and Operario, 2008) and telephone support services (Reynolds et al., 2008). But the use of these technology supported services may not be feasible in the West African sub region. Also the widespread use of adherence aids, such as pillboxes, counters or even timers have been shown to improve adherence (Golin et al., 2002).

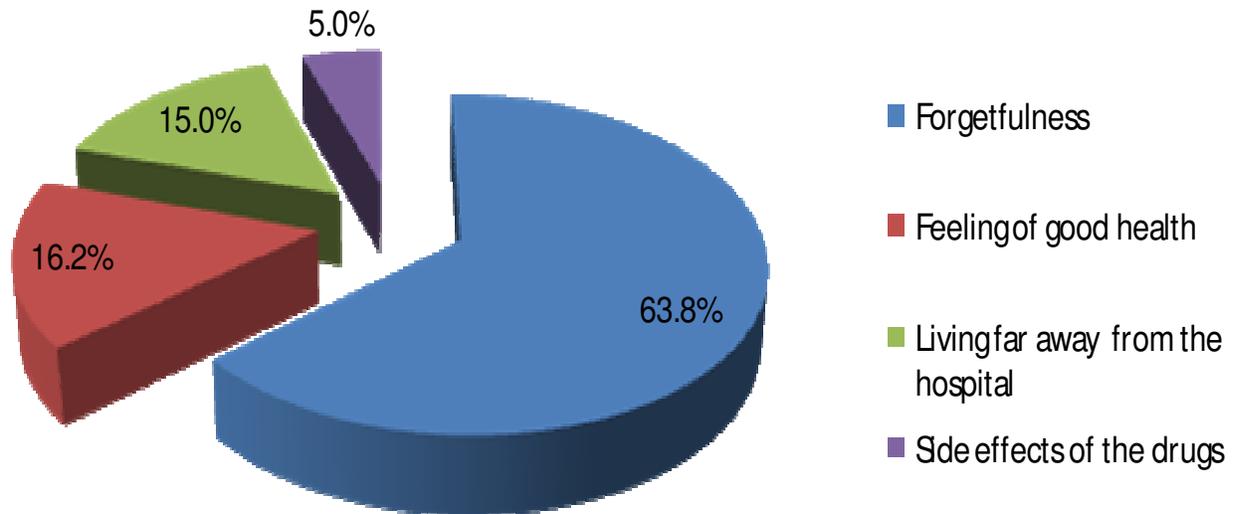
The other reasons found in this study include feeling healthy and living far away from the hospital. Patients living far from the hospital were likely to miss drug doses as they missed clinic attendance because they could not afford high cost of transportation. Bringing services to the doorsteps of the patients by expanding the existing facilities may improve patients' adherence to therapy. In other parts of Africa shortage of food has been reported as a major reason for non adherence to ARTs as these drugs were said to increase appetite (Hardon et al., 2006).

From our study, low educational level of the respondents, and their husbands' were associated with increased likelihood of non-adherence to therapy. This is in line with a previous report from Kano, northern part of

**Table 3.** Influence of socio-demographic factors on non-adherence to HAART among HIV-positive pregnant mothers at PMTCT clinic, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria.

Parameters	Non-adherent (%)	Adherent (%)	$\chi^2$	OR	df	P-value
<b>Age( years)</b>						
20-29	24(13.7)	151(86.3)	13.61		2	0.001*
30-39	49(29.0)	120(71.0)				
≥40	8(33.0)	16(67.0)				
<b>Parity</b>						
0-1	34(28.3)	86(71.7)	11.32		2	0.03*
2-4	31(15.5)	169(84.5)				
≥5	16(33.3)	32(66.7)				
<b>Marital status</b>						
Married	70(20.8)	267(79.2)	3.60	2		0.17
Single	9(36.0)	16(64.0)				
Widow	2(33.3)	4(67.7)				
<b>Formal educational level</b>						
No formal	8(100.0)	0(0.0)	39.36		3	0.002*
Primary	15(37.5)	25(62.5)				
Secondary	49(18.6)	215(81.4)				
Tertiary	7(12.5)	49(87.5)				
<b>Husband's educational level</b>						
Primary	25(38.5)	40(61.5)	13.75		2	0.01*
Secondary	45(18.4)	200(81.6)				
Tertiary	9(15.5)	49(84.5)				
<b>Occupation</b>						
Trading	31(15.0)	175(85.0)	64.02		4	0.001*
artisan	15(60.0)	9(40.0)				
Full time house wife	31(48.4)	33(51.6)				
Public servant	5(8.9)	51(91.9)				
Student	0(0.0)	16(100.0)				
<b>Partners' HIV-status</b>						
Negative	21(13.8)	131(86.2)	6.2		2	0.05*
Positive	45(24.5)	139(75.5)				
Unknown	7(21.9)	25(78.1)				
<b>Disclosure of HIV- status to partner</b>						
yes	61(18.8)	264(81.2)	12.96	0.29		0.003*
No	19(44.7)	24(55.8)				
<b>Duration of ART</b>						
0 - 2 yrs	30(14.8)	173(85.2)	9.52	0.44		0.001*
Above 2 yrs	47(28.5)	118(71.5)				
<b>Diagnosis</b>						
In pregnancy	6(9.4)	58(90.6)	5.21	0.35		0.02*
Before pregnancy	70(23.0)	234(77.0)				

\*Significant.



**Figure 1.** Reasons for non adherence to HAART among HIV-positive pregnant mothers at PMTCT clinic in Nnamdi Azikiwe University Teaching Hospital Nnewi, Nigeria (n = 80).

Nigeria where patients with formal education were found four times more likely to be adherent than those without formal education (Iliyasu et al., 2005). A similar finding was also documented in India, where patients with lower education reported lesser degree of adherence (Sarna et al., 2008). Low educational level is also associated with poor empowerment hence, females who were artisans and full time house wives were non-adherent to therapy. All the students were adherent. This underscores the pivotal role of education in reproductive health. Education may impact on adherence in several ways including facilitating communication with health workers, increasing retention of information provided by health workers, and thereby enhancing implementation of the recommendations regarding intake of the antiretroviral drugs.

The association of non-adherence to ART and nondisclosure of HIV status had been documented (Stirratt et al., 2006). Generally, serostatus disclosure is very important in the efforts at limiting the spread of HIV infection including prevention of MTCT and is therefore, currently emphasized by both WHO (UNAIDS, 1997) and the Centers for Disease Control and Prevention (2002) in their protocol for HIV counseling and testing. With disclosure, there is increased social and psychological support for the infected partner. In addition, disclosure may lead to improved access to HIV prevention and treatment programmes, as well as increased opportunity for risk reduction strategies including the use of condom among sexual partners. In West Indies, women who had disclosed their HIV status were more likely to use condoms during all sexual encounters, less likely to have had subsequent pregnancy from a different sex partner, more likely to have a partner who had been tested for HIV, and more likely to be attending the HIV clinic for

follow-up and care compared to those who did not disclose (Kumar et al., 2006). Our findings underscore the need to beef up efforts aimed at encouraging serostatus disclosure among people living with HIV/AIDS.

It was also observed that women who had been on ART for up to two years and beyond were more likely to be non-adherent. Increasing maternal age, and extremes of parity associated with non-adherence could also be related to longer duration of therapy. Expectedly, patients who commenced therapy newly are usually enthusiastic and therefore tend to comply with treatment more than those who had been on therapy for a long time. Therefore, there is need to continue regular adherence counseling for patients on ART. However a study from Zambia, an African country reported a higher adherence rate for those on ART for a long time, and a lower non adherence rate of 16.3% (Carlucci et al., 2008).

A surprising finding from this study is the association of non-adherence and seroconcordance. People in concordant relationships are expected to adhere more to therapy than those in serodiscordant relationship because of increased partner support. This occurrence may be as a result of complacency and poor motivation.

The use of patients self-report of skipped doses may be subject to recall bias. However studies have shown that self-report data correlate well with clinical, virologic and immunologic states (Sethi et al., 2003; Spire et al., 2002; Chesney et al., 2000). Also, this study did not correlate adherence rate with either viral load test or CD4 count used in monitoring the disease progression. Further studies to relate adherence to these tests is recommended.

In spite of these limitations, the findings from this study will be very useful in designing strategies to strengthen adherence counseling in the PMTCT programme of

this country.

## Conclusion

The study showed a high prevalence of non adherence to ARV drugs among the pregnant HIV-positive mothers caused mainly by forgetfulness and patients' feeling of good health. The determinants of non-adherence include low level of education, non-disclosure of HIV status and longer duration of therapy. The knowledge of these identified factors should be properly utilized and addressed during adherence counseling programmes. The adherence counseling programmes should also be regular and sustained for all patients on antiretroviral therapy for its optimal benefits.

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