



**Quantitative and Qualitative Adherence to HAART in Thar (Rajasthan) –A Six Months Follow-up Study.**

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**Introduction:** Adherence to HAART is an important issue regarding the treatment outcome. In India, after initiation of free ART supply by NACO, adherence studies must be needed from various corners of the country.

**Objectives:** To determine adherence to HAART in HIV/AIDS patients registered with the newly established NACO-ART Centre at Sardar Patel Medical College and Associated Group of Hospitals, Bikaner, Rajasthan.

**Methods:** It was six months follow up study on 120 patients. ARV drugs were supplied free of cost by NACO. Dedicated adherence counseling and support of the peer group, i.e., is, PLHA was its necessary part. The treatment strategy for all patients was 2 NRTI + 1 NNRTI. Adherence was calculated by the clinic based pill counts and further assessed by Self Report Questionnaire.

**Results:** 52.50% of the patients received AZT+3TC+NVP, 37.50% d4T+3TC+NVP and only 5.83% and 4.16% of patients were on AZT+3TC+EFV and d4T+3TC+EFV respectively. 62.5% were males and 37.5% were females. 59.66% of the patients were in age group of 30-45 yrs. The overall mean quantitative adherence was 92.14% (SD  $\pm$  5.77). 94 patients (78.33%) reported high Adherence i.e.  $\geq$ 90% and 26 patients (21.66%) reported low adherence i.e. < 90%. Adherence was dynamic over time, maximum at the first visit (93.70%) and minimum at second visit (89.60%). The most common reason reported for missing of doses was simply forgotten (56.47%), followed by busy in other things (15.29%).

**Key words:** Adherence, HAART, Follow-up, Qualitative, Quantitative, Thar desert.



## INTRODUCTION

WHO states the adherence as “The extent to which a person’s behavior-taking medication, following a diet and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider”<sup>1</sup>. Non-adherence is common particularly with long term treatments for conditions. A number of rigorous reviews have found that in developed countries adherence among patients suffering from chronic disease average only 50%<sup>2</sup>.

In the treatment of HIV/AIDS, it varies between 37% to 83% depending on the drug under study and the demographic characteristics of patient populations<sup>3</sup>. According to WHO, in developing countries, adherence to HAART is 60-80%<sup>1</sup>. When adherence rate is between 50-85%, the resistance towards ART is likely<sup>4</sup>

However, most of the studies are conducted in developed western countries and there is scarcity of data from developing countries where the affected population burden with HIV/AIDS is much greater than the western world and contrasting differences exist in socio-economic and educational parameters from that of the developed world.

## OBJECTIVES

To determine the adherence pattern to HAART in HIV/AIDS patients registered with the newly established NACO-ART Centre at Sardar Patel Medical College and Associated Group of Hospitals, Bikaner, Rajasthan.

## METHODS

This was a cohort study on adherence of HAART regimen in HIV/AIDS patients registered with the newly established Anti Retroviral Treatment Center (ART-C) at Associated Group of Hospitals, Bikaner, Rajasthan by the National AIDS Control Organization (NACO), Ministry of Health and Family Welfare, Government of India. At the commencement of study around 260 HIV patients were registered for ART out of which 120 patients were recruited for the study and were followed for six months.

The study was started in September 2008 and data collection was over till completion of six months follow-up of all patients in April 2009. The study was approved by the Ethical Committee of S.P. Medical College, Bikaner. As this ART center comes under the national program, dedicated adherence counseling by the professional counselor and support of the peer group, that is, Bikaner Network of PLHA (people living with HIV/AIDS) was a necessary part of it.

The use of NACO supplied (free of charge) antiretroviral drugs<sup>5</sup> was employed in the study, which did not include any protease inhibitors. The treatment strategy for all patients was inclusion of two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse transcriptase inhibitor (2 NRTI + 1 NNRTI).

Inclusion criteria for the patient:-

- Adults i.e.  $\geq 18$  years of age were included.
- Patients who were on ART for at least 1 month were included.

In this cohort study, the patients were given full details of the study method and then only written informed consent taken.

They were provided Self Report Questionnaire from Adult AIDS Clinical Trials Group (AACTG)<sup>6</sup> which was modified, further simplified and translated in Hindi to make it more culturally adoptable and understandable for the common man.

Qualitative adherence Q<sub>A</sub> - The two parameters related to qualitative adherence were assessed. Questions were asked related to the respect of prescribed time and respect of special instructions over last four days with answers to be given in five alternative choices. The percentage of full respect of prescribed time and special instructions were compared in the two groups of high and low adherence.

Detailed clinical examination was done by physician. To assess the adherence and to monitor the therapy, WHO clinical stage was assessed by the physician at every visit.

#### Quantitative Adherence - (Q<sub>N</sub>A)

Quantitative adherence was judged by the clinic based pill counts.

It was calculated as follows<sup>7</sup>: –

$$\text{Quantitative Adherence} = \frac{\text{Total number of pills taken}}{\text{Total number of pills prescribed}} \times 100$$

At a time the medications were given for a period of 30 days. The patients were followed monthly for a period of six months. The patients were told to bring their remaining pills at every scheduled visit. The patients who failed to bring their remaining pills (and thus making pill count impossible) were assigned 0% adherence as in adherence study by Orrell et al<sup>7</sup>. So, the adherence was calculated every month to have six reading for each patient.

#### STATISTICAL ANALYSIS

Means and standard deviations were calculated for continuous variables. The difference between the initial and final CD4 counts and weight in high and low adherent patients was analyzed by paired t test. The difference between the initial and final clinical staging, functional status in high and low adherent patients was analyzed by chi square test. The P value of less than 0.05 was considered significant.

#### OBSERVATIONS

Total 120 patients were enrolled for the study. 62.5% were males and 37.5% were females. 59.66% of the patients were in age group of 30-45 yrs, 27.50% of patients in age group of 18-30 yrs and 13.33% patients were above 45 yrs of age.

In present study 52.50% of the patients received AZT+3TC+NVP, 37.50% d4T+3TC+NVP and only 5.83% and 4.16% of patients were on AZT+3TC+EFV and d4T+3TC+EFV respectively.

Table I: Demographic characteristics (n=120)

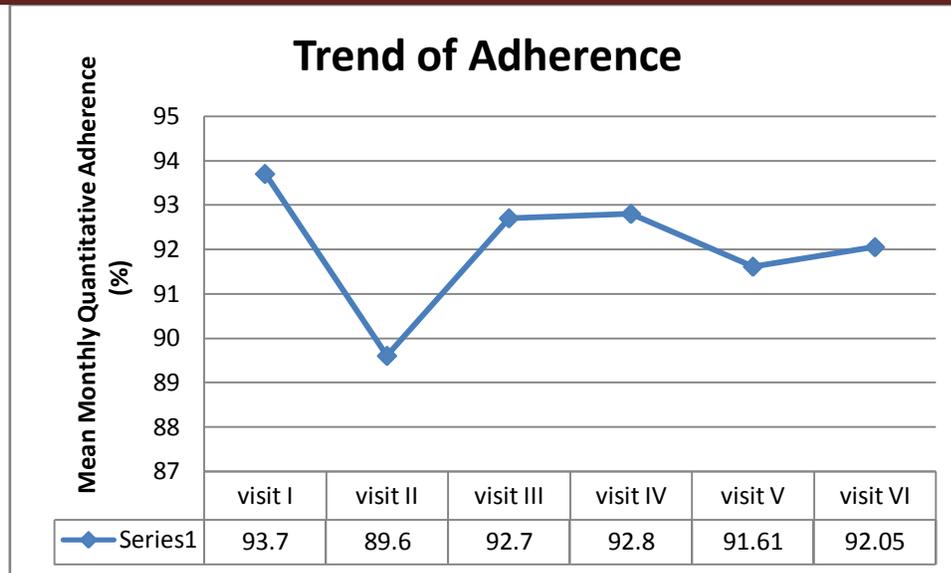
Sex	n	%
Male	76	62.50%
Female	44	37.50%
Age (yrs)		
18 – 30	33	27.50%
30 – 45	71	59.66%
Above 45	16	13.33%
ART Regimen		
AZT+3TC+NVP	63	52.50%
d4T + 3TC+NVP	45	37.50%
AZT+3TC+EFV	07	05.83%
d4T + 3TC+EFV	05	04.16%

At the start of study, the CD4 count of all the patients varied from 18 cells/microL. to 840 cells/microL. The mean CD4 count was 252.9 cells/microL. Initially, 79.66% patients were categorized in I and II WHO clinical stage where as only 20.88% patients were categorized in III and IV stage.

#### Quantitative Adherence ( $Q_{NA}$ )

The adherence readings were obtained for each patient at every monthly visit, so a total of 719 adherence months were obtained, as one female patient died after fifth visit. Ten patients at one of their six visits forgot to bring their pills back, making pill count impossible, so they were assigned 0% adherence for that visit.

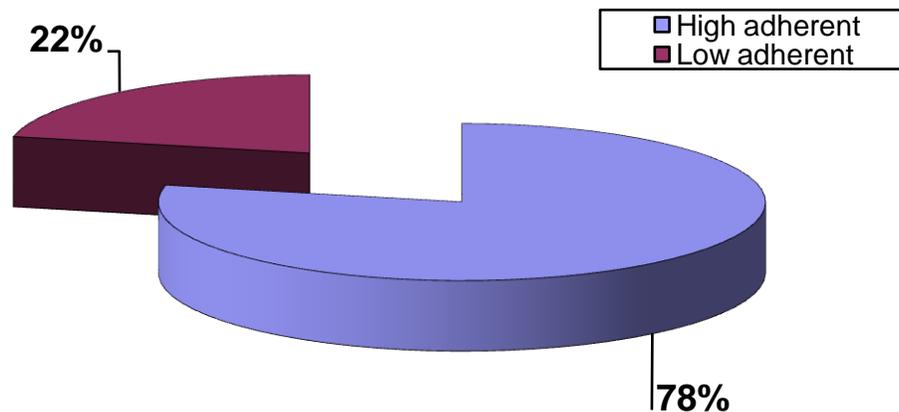
The mean of the monthly Quantitative Adherence  $Q_{NA}$  of each visit of all patients, i.e,  $mV_I Q_{NA}$ ,  $mV_{II} Q_{NA}$ ...  $mV_{VI} Q_{NA}$  was taken and then plotted over time. The mean of the monthly Quantitative Adherence  $Q_{NA}$  was not constant over time, maximum at the first visit (93.70%) and minimum at second visit (89.60%).



The overall mean quantitative adherence was 92.14% (SD  $\pm$  5.77). The Mean Quantitative Adherence (MQ<sub>N</sub>A) for each patient was calculated. 94 patients (78.33%) reported high Mean Quantitative Adherence i.e.  $\geq$ 90% and 26 patients (21.66%) reported low Mean Quantitative adherence i.e.  $<$  90%.

Figure: I

Distribution of patients according to adherence



The most common reason reported for missing of doses was simply forgotten (56.47%) in around 96 adherence months.

Table II: Reasons for missing of doses

Reasons	Adherence Months	Percentage(%)
Forgot	96	56.47
Busy in other things	26	15.29
Away from home	17	10
Ran out of pills	7	4.12
Wanting to avoid	7	4.12
Side effects Felt sick or ill	5	2.94
Had problem in taking pills at specified times (with meals on empty stomach, etc.)	5	2.94
Had a change in daily routine	3	1.76
Had too many pills to take	2	1.18
Felt asleep or slept through dose time	1	0.59
Difficulty in understanding	1	0.59
Difficulty in swallowing	1	0.59

The overall mean CD4 count at the commencement of the study was 252.9cells/microl. (SD  $\pm$  173.8). The overall mean CD4 count after completion of the study was 330.52 cells/microl. (SD  $\pm$  187.82). In high adherent patients (n=94), the mean initial CD4 count was 267.27 cells/microl. (SD $\pm$ 171.64) and mean final CD4 count was 368.15 cells/microl. (SD $\pm$ 179.34). The increase in the CD4 count in high adherent patients was very highly significant ( $p < 0.001$ ). Among low adherent patients, mean initial CD4 count was 200.92 cells/microl. (SD  $\pm$ 175.18) and mean final CD4 count was 189.04 cells/microl. (SD  $\pm$  149.69). The decrease in the CD4 count was not significant ( $p > 0.05$ ).

Table III: Adherence and change in CD4 count

	High Adherent	Low Adherent
Initial CD4 count	267.27 $\pm$ 171.64	200.92 $\pm$ 175.18
Final CD4 count	368.15 $\pm$ 179.34	189.04 $\pm$ 149.69
t	3.94	0.24
P	P < 0.001	P > 0.05

The increase in weight in the high adherent patients was significant ( $p=0.05$ ). In low adherent patients also, the increase in weight was observed but the difference was not significant ( $p > 0.05$ ).

Table IV: Adherence and change in Weight

	High Adherent	Low Adherent
Initial Weight	52.22 $\pm$ 9.61	55.73 $\pm$ 12.39
Final Weight	54.89 $\pm$ 9.58	58.28 $\pm$ 11.97
t	1.90	0.75
P	$P \leq 0.05$	$P > 0.05$

Initially 68 patients were classified in WHO clinical stage I among high adherent patients. At the end of study 87 patients were classified in clinical stage I. The overall difference in initial and final clinical staging was highly significant ( $p < 0.01$ ). Among low adherent patients, initially 16 were classified in stage I and at the end of study 20 were classified in stage I. The overall difference in initial and final WHO clinical staging among low adherent patients was not significant ( $p > 0.05$ ).

Table V: Adherence and Change in WHO Clinical Stage

Clinical Staging	High Adherent				Low Adherent			
	I	II	III	IV	I	II	III	IV
Initial	68	11	11	4	6	0	5	5
Final	87	4	2	1	20	1	0	4
$\chi^2$	13.62				6.53			
P	$< 0.01$				$> 0.05$			

Qualitative Adherence ( Q<sub>L</sub>A)

For every patient the degree of qualitative adherence was assessed at every visit. Thus 719 readings for the parameters, that is, the respect of prescribed time and the respect of regimen instructions were obtained. The total percentage of the 100% respect of prescribed time was 29.90% and of the 100% respect of regimen instructions was 29.49%. Whereas, the percentage of the 100% respect of prescribed time was 37.06% and 3.87% in high and low adherent groups respectively; and the percentage of the 100% respect of regimen instructions was 36.70% and 3.23% in high and low adherent groups respectively. The difference in the 100% respect of both the parameters in the two groups was highly significant ( $p < 0.001$ ).

Table VI: Qualitative Adherence and quantitative adherence

Qualitative adherence	High	Low	$\chi^2$	P
Respect of prescribed time	37.06 %	3.87%	63.88	<0.001
Respect of regimen instructions	36.70%	3.23%	62.48	<0.001

## DISCUSSION

The results of the present study showed high level of overall mean adherence i.e. 92.14%. High adherence was reported in our study in 78.33% patients. In contrast to this Paterson et al<sup>8</sup> observed low levels of adherence. The findings were similar to the studies done by Orrell et al<sup>7</sup> and Etard et al<sup>9</sup> as regards the level of adherence and percentage of patients showing high adherence. Furthermore, our results fairly matched with two Indian studies,<sup>10,11</sup> which also reported the mean adherence more than 90% and above 80% patients reported higher adherence. This high level of adherence can be attributed to dedicated adherence counseling and regular monthly clinic based pill count as illustrated by Parry et al<sup>12</sup> and Achieng et al<sup>13</sup>, respectively. Lal et al<sup>14</sup> and Byakika-Tusiime et al<sup>15</sup> also supports the high adherence finding in free ART distribution set-up.

Ours is an Indian study representing developing country showing high level of adherence which can be visualized by the meta-analysis done by Mills et al<sup>16</sup> suggesting lower level of pooled adherence in North American studies and higher level of pooled adherence in African studies.

The above differences in adherence could be explained in the following manner :-

- 1 In developing countries the most common measures of adherence used were pill counts (mostly clinic based) and/or self report questionnaires, which usually report higher adherence, where as in developed countries most frequently employed measures were electronic devices.
- 2 The ART regimens in developing countries mostly comprised of fixed dose combinations of (NNRTI + 2 NRTIs) so the pill load reduces drastically to 2 or 3, where as the studies from developed countries included more frequent use of PI based regimens thus increasing the pill load to 10.

The trend of adherence in context with our study shows that during first visit patients adhere very well, followed by a decrease of adherence for next two months. There after in our study the adherence gradually increased however, it could not reach the initial high level. Almost the similar variations were observed by Howard et al<sup>17</sup> and Etard et al<sup>9</sup>. Recently also, Wilson et al<sup>18</sup> in a multisite adherence collaboration study found heterogeneity among studies in rates of decline of ART adherence and its non linear nature over time.

In support of the previous studies<sup>8,12,19,20</sup>, the present study showed significant ( $p < 0.001$ ) increase in CD4 counts (i.e. increase of 101 cells/ $\mu$ l) among high adherent patients, while insignificant change amongst low adherent patients.

In concordance with the study by Mwamburi and associates<sup>21</sup> which examined the association between virus load and body weight and the impact of HAART use concluded that for the patients who had detectable virus loads and were already taking HAART, changes in adherence or changes in the HAART regimen were likely to result in weight gain, if there was an accompanying increase in CD4 cell count; the present study also observed significant association of mean increase in weight (i.e. 01.67 Kg,



p=0.05) and high adherence. Significant improvement in WHO HIV clinical staging among high adherence patients was also noticed.

The reasons for missing of doses by the patients were tally with the other studies<sup>12,22,23,24,25</sup>. In our study forgetting, being busy with other things and away from home were cited as the most common reasons.

Qualitative adherence was judged on the basis of respect of prescribed time and regimen instructions in the last four days. The 100% respect of the prescribed time was 29.90% and 100% respect of the regimen instructions was 29.49% only. Whereas a study from Cote d'Ivoire<sup>19</sup> found that 63.6% patients took their medication at prescribed time and 76.2% followed regimen instructions. However, in concordance with the present study, Sarna et al<sup>11</sup> found that 39.7% of the patients receiving free ART, followed ARV medication schedule closely in about four days.

#### CONCLUSION

The general conclusion drawn from the above findings is that high adherence i.e., 92.14% was observed in most of the patients i.e., 78.33 %. The high adherence was translated favorably as regards immunologic (CD4 counts) and clinical outcomes (WHO HIV clinical staging, weight gain). Thus, it can be stated from over study that good adherence is a valid region for the improvement in CD4 count.

The adherence has shown dynamic behavior over time in our study. It was maximum at the first visit and then a dip was observed. Thereafter, it increased but not up to the initial level.

As the most common reason seen for missing of doses in our study was 'forgetting', it is proposed that the adherence can be improved by implying memory measures (medication diaries, weekly pill boxes, pagers, alarms, beepers etc) and providing special attention in such patients. Last but not the least the need of qualitative adherence i.e. to follow regimen instructions and timing of doses should also be emphasized.

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