



# The Relationship between Drug Adherence to Antiretroviral Therapy and Viral Load in Children Living with HIV

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## Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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## ABSTRACT

**Introduction:** HIV infection is one of the major public health issues in India and globally. Adherence to ARV drugs is important for optimal virological suppression and should be assessed routinely and strictly reinforced. There is limited information on adherence patterns and its determinants in children in resource-constrained countries because these countries have limited options if viral resistance develops. The objective of our study was to determine the relationship between viral load and drug adherence in children living with HIV and to determine socio-demographic factors affecting adherence and reasons for non-adherence.

**Materials and Methods:** In this cross-sectional observational study, 70 children on ART were enrolled after applying the inclusion and exclusion criteria. All clinical, demographic details and investigations available were noted. Adherence was assessed by the pill counting method. Caregivers who reported missing doses were given the pediatric nonadherence questionnaire. Blood sample was analyzed for viral load estimation. Appropriate statistical tests were used and analysis was done.

**Results:** The mean age of diagnosis in study subjects was  $8.13 \pm 3.89$  years and mean duration of treatment was  $4.24 \pm 3.05$  years. Majority, 61(87.1%) patients had adherence more than 95%. Among 9 non-adherent children, the main reason was that they forgot to take medicine in 8(88.9%)

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cases. The adherent group had significant virological suppression and higher CD4 count. Mean viral load in the adherent group was  $2379 \pm 5996.74$  copies per ml against  $46529.22 \pm 86633.12$  copies per ml in the non-adherent group.

**Conclusion:** We found that adherent group had a higher CD4 count and a suppressed viral load and adherence to ART was unrelated to age, sex, duration of HIV infection and treatment, socioeconomic status, and route of transmission.

**Keywords:** CLHIV; ART; adherence; pill counting; viral load; CD4 count.

## 1. INTRODUCTION

HIV infection is one of the major public health issues in India as well as globally. WHO data suggests that among 37 million people living with HIV, approx. 2.6 million are children [1]. India has the largest number of AIDS orphans as suggested by data from the Joint United Nations Program on HIV/AIDS [2].

Studies have shown that Pediatric HIV has now become an epidemic in India as well as in many parts of the world as children born with perinatal HIV infections are reaching adolescence and adulthood due to increased use of highly active antiretroviral therapy (HAART) and optimal adherence to ART has played a key role in achieving this milestone.

Studies both in adults and children have demonstrated that a high level of adherence is essential as there may be a rapid emergence of resistant mutations, leading to treatment failure, re-emergence of opportunistic infections and disease [2,3].

A systematic review (2007) documented mean adherence of 88.4–96% in children [4]. Still, there is limited data on adherence patterns and its determinants in children from resource-constrained nations like India with high HIV prevalence [5-7].

There are many factors which can influence adherence to ART in children such as medication, caregivers, and health facility. Thus sound knowledge of these factors can help to optimize adherence in children as non-adherence to treatment results in the development of viral resistance, treatment failure, and increased risk of disease progression. Hence, such cases would require increased use of second-line and salvage regimens, which are in general more expensive than initial regimens as suggested by public health economics [8].

Meanwhile, the WHO 2010 and 2013 guidelines proposed the utility of viral load to discriminate the patient who needs adherence support and those to be started on second-line ART. So, the viral load remains the gold standard for monitoring the efficacy of HIV treatment and measuring the validity of adherence reports [5,9–11].

The National AIDS Control Organization (NACO) launched the National Paediatric HIV Initiative in November 2006 in India, to rapidly scale up access to care, support, and treatment for pediatric patients across the country. Under this program, the government provides ART at free of cost to all HIV-infected children. Thus, after five years of this nearly 76,600 HIV-infected children are registered in HIV care, of which 21,665 are receiving ART in India (National AIDS Control Organization. Care support and treatment, 2012)

### 1.1 Aims and Objectives

#### 1.1.1 Aim

To study the relationship between viral load and drug adherence in children living with HIV.

#### 1.1.2 Primary objective

To determine the relationship between viral load and drug adherence in children living with HIV.

#### 1.1.3 Secondary objective

1. To determine socio-demographic factors affecting adherence.
2. To determine common reasons for nonadherence

## 2. MATERIALS AND METHODS

### 2.1 Place of Study

This study was conducted at the Department of Pediatrics ART Clinic ABVIMS and Dr. Ram Manohar Lohia Hospital, New Delhi-110010.

## 2.2 Subjects

Children who were follow up cases at the Pediatric ART clinic of ABVIMS and Dr. Ram Manohar Lohia Hospital receiving ART more than six months after consent from caregiver and assent of children wherever possible.

### 2.2.1 Study design

Cross-sectional observational study

### 2.2.2 Study period

1<sup>st</sup> November 2018-31<sup>st</sup> March 2020

## 2.3 Inclusion Criteria

- Children with HIV >6 months of HAART(Highly Active Antiretroviral Therapy)
- Children aged 5-18 year
- Children reporting with caregiver
- Children not infected with any other chronic disease such as hepatitis B and C

## 2.4 Exclusion Criteria

- Children those on second line ART
- Children with terminal illnesses
- Children who lost family recently<3 months
- Children whose caregiver is hospitalized with some critical illness.

## 2.5 Methodology

This study was conducted at Dr. Ram Manohar Lohia Hospital a tertiary care teaching hospital in New Delhi. At our center, the children living with HIV (CLHIV) were provided with comprehensive HIV care including ART at free of cost according to the latest guidelines by the National AIDS Control Organization (NACO). The antiretroviral (ARV) drugs were available in the form of dispersible, fixed-dose combination tablets that are dispensed on a monthly course.

All children 5 to 18 years of age registered at the clinic, on ART for at least 6 months, under follow-up at the clinic during the study period, and accompanied by a caregiver were included in the study. Children with terminal illnesses or incapacitated caregivers were excluded.

The primary caregiver was identified. A primary caregiver is defined as the person who takes the overall responsibility of giving/supervising the medication to the child in certain cases it could be the child himself/herself.

Data on the patient's age, duration of HIV infection and antiretroviral therapy, pre-antiretroviral WHO clinical stage and CD4 count, viral load levels, and ART regimen was obtained from patient records maintained at the clinic. The caregivers were asked about their educational status and employment and the child's parental HIV status and ART intake, orphan status, cause of parental death, type of family, and school enrolment.

For children enrolled under this, the drug, adherence was assessed by the pill counting method

## 2.6 Pill Counting Methods

Adherence was assessed at the visit by the pill count method. The patients were given a calculated number of pills every month based on the prescribed dose and the caregivers will bring back the pillbox with the leftover pills. Adherence was assessed by counting leftover pills. Adherence percentage is then calculated as:

$$\frac{\text{Number of pills taken by the patient}}{\text{Number of pills expected to be taken}} \times 100$$

A patient is considered adherent if he or she takes  $\geq 95\%$  of the prescribed medication and < 95% was called nonadherent. Caregivers who reported missing doses were given the pediatric nonadherence questionnaire.

## 2.7 Viral Load

The blood sample was sent for viral load estimation in the microbiology lab of ABVIMS and Dr. Ram Manohar Lohia hospital and the following process was followed.

## 2.8 Nucleic Acid Extraction of viral RNA

The extraction process was done on 'NuclieSENS easyMAG'nucleic acid extraction system(biomerieux)

This was done in 4 steps after the sample placed in the machine:

**Chart 1. Pediatric Adherence Questionnaire Module 2- Revised General Reasons For Non-adherence**

Reasons for Non-adherence	Yes	No
a. Can't get drug (drug store doesn't have supply)		
b. Didn't refill; ran out		
c. Taste, can't get it down, spits up, amount (pills or liquid)		
d. Forgot		
e. Caused physical effects (rash, pain, headache, etc.)		
f. Scheduling - Interferes with lifestyle (meals, school, sleep)		
g. Child refuses		
h. Multiple caretakers		
i. Concerns about disclosure		
j. Sick with other illness		
k. Doesn't remember/not sure if dose was taken		
l. Fell asleep		
m. Away from home		

1. Lysis step-nucleic acid release and stabilization
2. Silica binding
3. Washing-removing the inhibitor by washing
4. Elution-pure nucleic acid extracted after removing silica with an elution buffers

CT value determines the presence of the HIV virus.

The CT value was analyzed for the calculation of positive and negative results along with the quantitative estimation of RNA copies.

Data thus collected was used to find the correlation between the pill count method of adherence and viral load through statistical analysis.

## 2.9 RT-PCR Amplification

Extracted nucleic acid material was subjected to RT-PCR amplification by 'Rotor GeneQ' equipment by Qiagen.

A master mix was prepared by using HIV PCR solution, Taq DNA polymerase, UNG and extracted DNA.

The mix was placed in Rotor-Gene Q equipment.

CT value was calculated for the samples as per the manufacturer's instructions.

CT(cycle threshold) is defined as the number of cycles required for the fluorescent signal to cross the threshold.

## 3. RESULTS

### 3.1 Demographic Profile

In our study, HIV positive children from age group 05-18years and their caregivers were enrolled from the ART clinic. The youngest child was 5 years of age and the eldest was 18 years, mean age being  $12.57 \pm 3.31$  years.

### 3.2 Sex Distribution in the Study Population

It was observed that out of 70 children, majority of them, 44(62.9%) were males while 26(37%) were females.

**Table 1. Gender**

Gender	Number	Percentage
Male	44	62.9
Female	26	37.1
Total	70	100.0

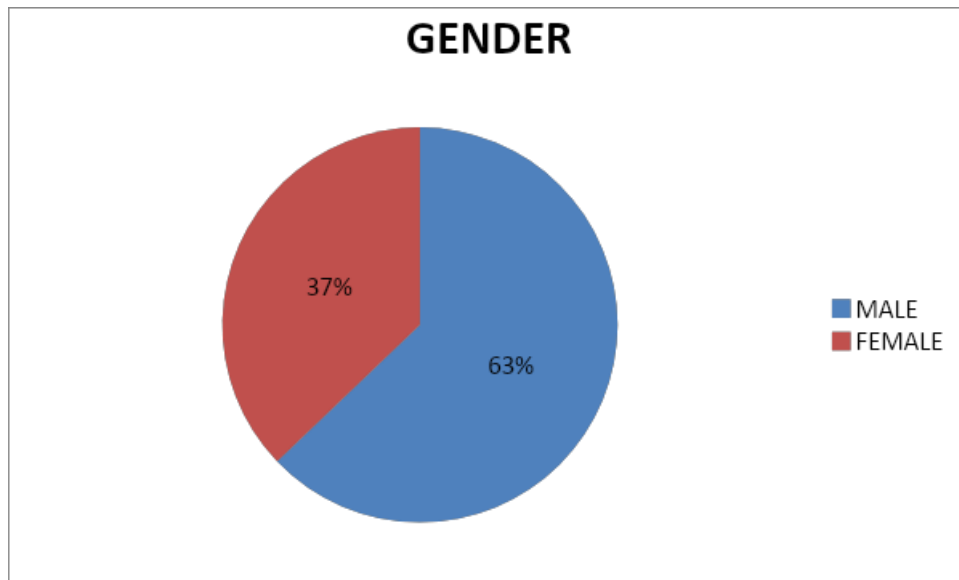


Fig. 1. Gender

Table 2. Age distribution of study population

Age group	Number	Percentage
5 to 9	13	18.6
10 to 18	57	81.4
Total	70	100.0

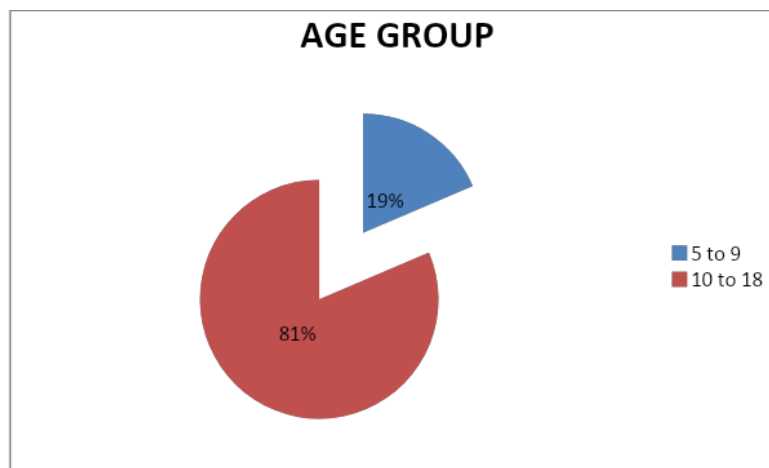


Fig. 2. Age group

### 3.3 Age Distribution of Study Population

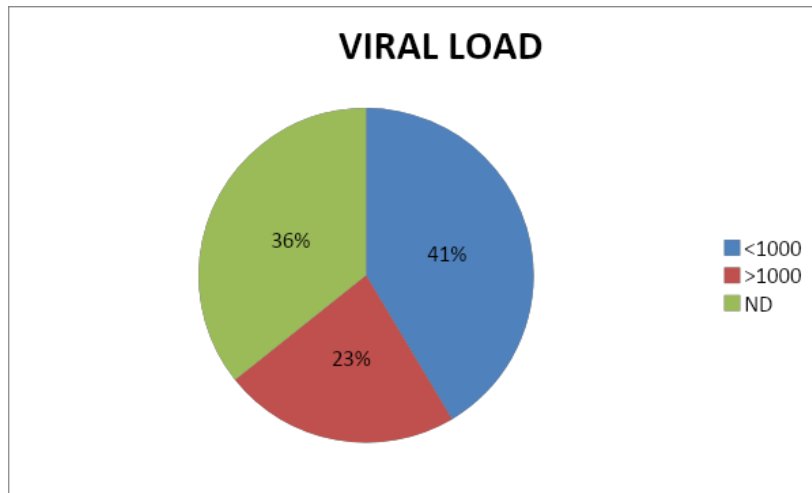
In our study population of 70 children, 57(81.4%) were in the age group of 10 to 18 years and 13(18.6%) were in the age group of 5 to 9 years.

### 3.4 Viral Load in the Study Population

Among 70 children 54(77.1%) were having copies less than 1000copies/ ml out of which 25(35.7%) had undetectable viral load. 16(22.9%) were having more than 1000 copies/ml.

**Table 3. Viral Load**

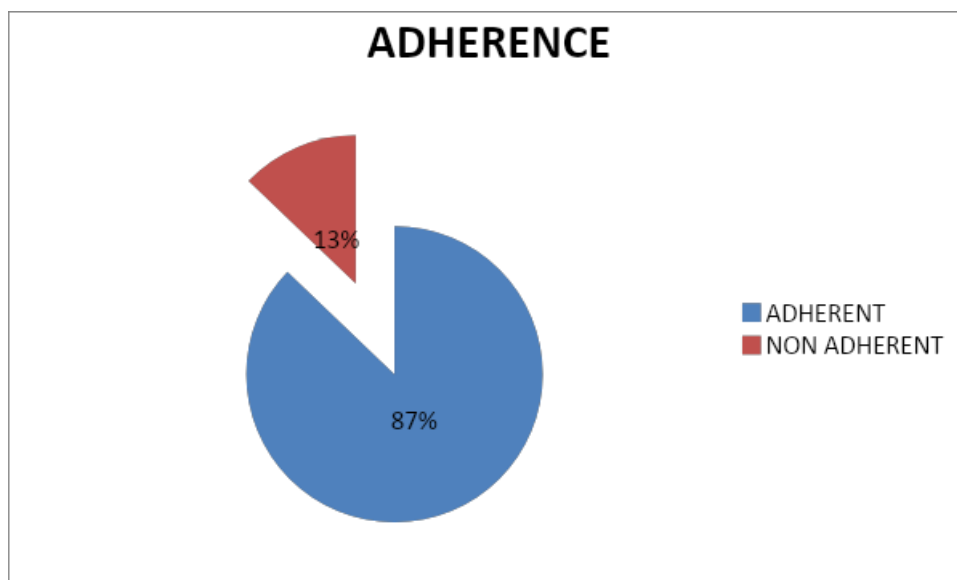
<b>Viral Load</b>	<b>Number</b>	<b>Percentage</b>
<1000	29	41.4
≥1000	16	22.9
ND	25	35.7
<b>TOTAL</b>	<b>70</b>	<b>100.0</b>



**Fig. 3. Viral Load**

**Table 4. Adherence**

<b>Adherence</b>	<b>Number</b>	<b>Percentage</b>
ADHERENT	61	87.1
NON ADHERENT	9	12.9
<b>Total</b>	<b>70</b>	<b>100.0</b>



**Fig. 4. Adherence**

### 3.5 Distribution of Study Population based on Adherence and Nonadherence to ART

Among the 70 children, 61(87.1%) had adherence more than 95% while 9 (12.9%) had adherence less than 95%.

### 3.6 Reason for Non Adherence

In our study of 70 children among 9 nonadherent patients the main reason for nonadherence was

that they forgot to take medicine in 8(88.9%) and 1 child (11.1%) was nonadherent because he did not like the medicine taste.

### 3.7 Distribution of CD4 Count among the Study Population

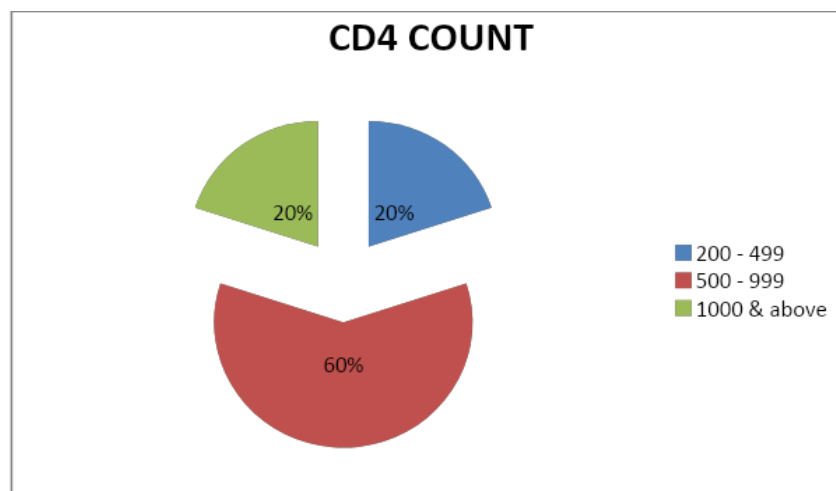
In our study of 70 children, 42(60%) had CD4 count in the range of 500 - 999 cells per cubic millimeter, however 14(20%) had CD4 count in the range of 299 -499 cells per cubic millimeter and is shown in Fig. 5.

**Table 5. Reason For Non Adherence**

Reason for non Adherence	Number	Percentage
Can't get drug (drug store doesn't have supply)	0	0.0
Didn't refill; ran out	0	0.0
Taste, can't get it down, spits up, amount (pills or liquid)	1	11.1
Forgot	8	88.9
Caused physical effects (rash, pain, headache, etc.)	0	0.0
Scheduling - Interferes with lifestyle (meals, school, sleep)	0	0.0
Child refuses	0	0.0
Multiple caretakers	0	0.0
Concerns about disclosure	0	0.0
Sick with other illness	0	0.0
Doesn't remember/not sure if dose was taken	0	0.0
Fell asleep	0	0.0
Away from home	0	0.0

**Table 6. Distribution Of Cd4 Count**

CD4 Count (cells per cubic millimeter)	Number	Percentage
200 – 499	14	20.0
500 – 999	42	60.0
1000 & above	14	20.0
Total	70	100.0



**Fig. 5. Distribution of CD4 count among the study population**

We found that,

The mean age in the adherent group was 12.46±3.38yr against 13.33±2.83yr in a nonadherent group with no statistically significant difference between the two groups (p value 0.464).

The mean age at diagnosis adherent group was 8.03±3.99yr against 8.78±3.27yr in the nonadherent group with no statistically significant difference between the two groups (p value 0.595).

The mean duration of HIV infection in the adherent group was 4.53±3.33 yr against 4.56±3.09yr in the nonadherent group with no statistically significant difference between the two groups (p value 0.985).

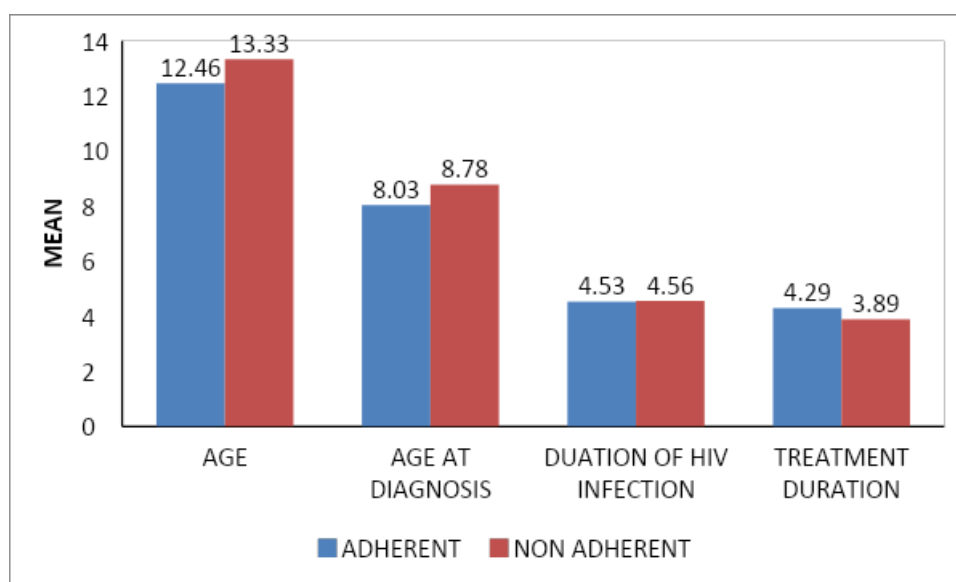
The mean duration of treatment in the adherent group was 4.29±3.16yr against 3.89±2.32yr in the nonadherent group with no statistically significant difference between the two groups (p value 0.713).

We found that, mean viral load in the adherent group was 2379±5996.74 copies per ml against 46529.22±86633.

THE mean CD4 count in the adherent group was 794±281 cells per cubic millimeter against 531±250 cells per cubic millimeter in the nonadherent group statistically significant difference between the two groups (p value 0.010).

**Table 7. Adherent and nonadherent group ratio**

Variables	Adherent		Non adherent		Unpaired t Test P Value
	Mean	SD	Mean	SD	
Age	12.46	3.38	13.33	2.83	0.464
Age at diagnosis	8.03	3.99	8.78	3.27	0.595
Duration of HIV infection	4.53	3.33	4.56	3.09	0.985
Treatment duration	4.29	3.16	3.89	2.32	0.718



**Fig. 6. Comparison of mean viral load and mean CD4 count among adherent and nonadherent group**

**Table 8. T-Test Results**

Variables	Adherent		Non adherent		Unpaired t test P value
	Mean	SD	Mean	SD	
VIRAL LOAD	2379.00	5996.74	46529.22	86633.12	0.005
CD4 COUNT	794.95	281.40	531.78	250.53	0.010



### 3.8 Comparison of Viral Load (quantitative) among Adherent and Nonadherent Groups

In our study of 70 children, a viral load of <1000 copies per ml was found in 28 (77.8%) in the adherent group and 1(11.1%) in the non-adherent group. Viral load copies >1000 copies per ml were found in 8(22.2%) among the

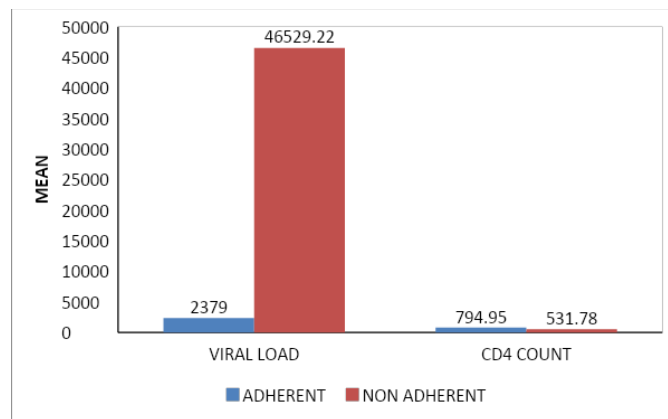
adherent group and 8(88.8%) in the nonadherent group.

There was a significant statistical difference between the two groups (p<0.001).

significant statistical difference was found between the adherent and nonadherent group (p value 0.011).

**Table 9. Chi-square Test**

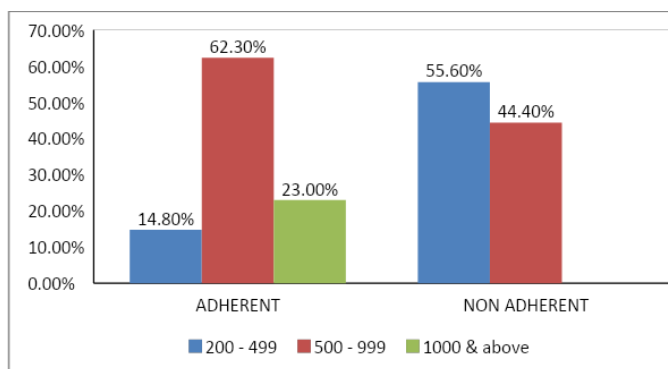
Viral load	Adherent		Non adherent		Chi-square test P value
	NO	%	NO	%	
<1000	28	77.8%	1	11.1%	<0.001
≥ 1000	8	22.2%	8	88.9%	
TOTAL	36	100.0%	9	100.0%	



**Fig. 7. Comparison of CD4 (quantitative) among adherent and nonadherent groups**

**Table 10. Chi-square Test Results**

Cd4 Count	Adherent		Non adherent		Chi-square test P value
	No	%	No	%	
200 – 499	9	14.8%	5	55.6%	0.011
500 – 999	38	62.3%	4	44.4%	
1000 & above	14	23.0%	0	.0%	



**Fig. 8. Comparison of CD4 (quantitative) cells among adherent and nonadherent groups**

## 4. DISCUSSION

### 4.1 Description of the Study Participants

It was a cross-sectional study in which 70 HIV positive children of age group 5-18 years attending ART clinic in ABVIMS and RML hospital were enrolled. Their proforma was filled which include demographic data, details of drug regime, WHO Staging, and adherence was calculated by pill counting method for those who had adherence less than 95 % were given a questionnaire for reasons nonadherence and to find out the reason for nonadherence.

Our study found that the children with an adherence of 95percent and above have less than 1000 HIV RNA copies per ml. We have measured the adherence using the pill counting (30 days) method at the time of pharmacy refill. Using the given formula:

$$\frac{\text{Number of pills taken by the patient}}{\text{Number of pills expected to be taken}} \times 100$$

Maintaining adherence to medication is a challenge in all diseases requiring long-term treatment, that too in case of children. It is well accepted that a sustained adherence to ART of >95% is required to maximally suppress viral replication [12] and prevent the emergence of drug resistance in individuals with HIV infection.

Among the 70 children in our study, 61(87.1%) cases had adherence more than 95% and 9 (12.9%) cases had adherence less than 95%. A systematic review of 13 studies by Simoni et al [4] has also reported a mean adherence ranging from 88.4% to 96% in children. Our results are also in agreement with this review.

Many factors have contributed to the high level of adherence to ART observed by us. The availability of comprehensive pediatric services related to HIV under one roof is a crucial factor. Similarly important is the availability of ART and other medication free of cost. The availability of child-friendly dispersible fixed-dose combinations of ART drugs has helped to limit the pill burden and dosing frequency and has improved palatability. Adherence to tablet formulations has been reported to be better than syrup formulations is shown by a study by Bagenda et al. [6]. Rigorous pre-ART counseling, ongoing adherence assessment, and supportive

counseling carried out routinely at our center further contribute towards maintaining adherence, so does an efficient system for contacting and recalling patients who miss a scheduled appointment. Some studies have reported a sub-optimal adherence in children [13,14]. In our study of 70 children, among the 9 nonadherent patients, the reason for nonadherence was that they forgot to take the medicine in 8(88.9%) children and in 1 case (11.1%), the child was nonadherent because he did not like the taste of medicine.

In our study population of 70 children, 57 (81.4%) cases were in the age group of 10 to 18 years and 13 (18.6%) children were in the age group of 5 to 9 years. The mean age in the adherent group was 12.46±3.38yr against 13.33±2.83ys in the non-adherent group with no statistically significant difference between the two groups (p value 0.464). Similar results were also found in Mehta. K et al (2015) [17], Bhattacharya et al (2011) [16], Seth. A et al (2013) [19] and Martelli et al (2019) [18] But the study done by Williams et al (2006) [15] found that children in the older age group were associated with decreased adherence and the reasons given were social issues, children taking responsibilities of their own medicines and normal challenges of adolescence. Our study was not in agreement with Williams et al because of regular counseling of the child and the caregiver at every visit to the ART center.

In our study, it was observed that out of 70 children, 44(62.9%) cases were males while 26(37%) cases were females and we found out that the gender of the child is not related to adherence which is consistent with findings of Mehta. K et al [17] (2015). The difference in our findings might be because at our ART centers regular counseling and psychosocial support are provided to every child through experienced counselors irrespective of the gender of the child.

In our study of 70 children, we found that the mean viral load in the adherent group was 2379±5996.74 copies per ml against 46529.22±86633.12 copies per ml in the nonadherent group with a statistically significant difference between the two groups (p value 0.005) and mean CD4 in the adherent group was 794±281 cells per cubic millimeter against 531±250 cells per cubic millimeter in the nonadherent group. A statistically significant difference was noted between the two groups (p value 0.010), here we found out that children with

Table 11.

S.No	Characteristics	Williams et al.[15] (2006)	Bhattacharya et al.[16] (2011)	Seth. A et al .[19](2013)	Mehta. K et al[17] .(2015)	Martelli et al.[18](2019)	Present study
1	<b>No of participants</b>	2088	90	106	164	72	70
2	<b>Age (years)</b>	13-18	1.5-11	6-12 (IQR 77.3-133.8 Months)	6.6-13.8	Less than 18 years	5-18
3	<b>Gender (Male)</b>	1012	56	76	95	33	44
4	<b>Type of study</b>	Cross Sectional	Cross Sectional	Prospective Observational Study	Cross Sectional	Cross sectional	Cross Sectional
5	<b>Method for measuring adherence</b>	<b>3 day recall</b>	4 Day Recall	3 day recall, pill counting	Visual analog scale (VAS), Self reporting method (missed doses per day during past 3 months, treatment interruptions for > 48 over last 3 months)	Pill count	Pill count
6	<b>Adherence &gt; 95 %</b>	<b>84%</b>	65.7%	3 Day pill recall - 99.1% Pill Count - 95.3%	90.9 %	65.3%	87%
7	<b>Immunological indicator used</b>	<b>CD4</b>	CD4	CD4	CD4	CD4	CD4
8	<b>Virological indicator used</b>	<b>Viral load(RNA copies)</b>	Not done	Not Done	Viral load(RNA copies)	Viral load(RNA copies)	Viral load(RNA copies)
9	<b>Viral load cut off (RNA copies per ml)</b>	<b>&gt; 400</b>	NA	NA	>400	> 1000	> 1000
10	<b>Results with respect to viral load and CD4</b>	Among 2088 children and adolescents, 84%	The rise inCD4 count after ART initiation was more	-	The proportion of children who experienced	62.5% and 65.3% of the individuals presented an	The adherent group was having

<b>count</b>	reported complete adherence to antiretroviral therapy medications over the past 3 days. The median viral load was 10 times higher among nonadherent than adherent children, and the strength of this association increased with age.	marked in the high adherence group, with the difference in the two groups becoming statistically significant after 6 months of ART	virological failure was 16.5 %. Virological failure was not linked to suboptimal adherence	optimal adherence according to viral load and pill count respectively, but among 40% viral load results diverged from the pill count method	significant virological suppression with a significantly higher CD4 count
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high adherence to ART are much better immunologically as they have higher CD4 count and a better viral suppression than their nonadherent peers. Martelli.et al (2019) [18] showed that CD4 count of more than 500 cells per microliters was significantly associated with optimal adherence. We could not find many studies showing results in mean CD4 count.

In our study out of 70 children, a viral load of <1000 copies per ml was found in 28 (77.8%) patients in the adherent group and was 1(11.1%) child in the non-adherent group. Viral load copies >1000 copies per ml were found in 8(22.2%) patients among the adherent group and 8(88.8%) cases in the nonadherent group the data was of significant statistical difference between the two groups ( $p<0.001$ ). We had the same finding as Williams et al [15] (2006). A study was done by Mehta. K et al (2015) [17] show despite such high reported rates of ART adherence, 15.4 % of their optimally adherent children did not achieve virological suppression. The results might have a difference because of cut off value of viral RNA copies per ml used in their study is 400copies per ml which is also not following the latest NACO 2018 guidelines which recommend more than or equal to 1000 copies per ml, and as the cut off is taken at a lower value so many children with a viral load between 400 and 1000 would have been reported under virological failure in this study, additionally, the study uses visual analog scale(VAS) representing past month adherence and treatment interruptions 48 h during the past 3 months as self reporting method of calculating adherence to ART which showed high adherence among study subjects but in our study, we have used pill counting method which is also a recommended method of self reporting according to NACO 2018 guidelines. A study by Martelli.et al [18] (2019) reported 62.5% and 65.3% of the individuals presented an optimal adherence according to viral load and pill count method respectively, but among 40% viral load results diverged from the pill count method, the results in this study was not the same with our study this might be because they had taken children with second line ART, which means they already resistant to first line ART. So they had not taken care of the resistance factor which we had taken into account in our study. African continent did not have enough resources such as food and nutrition and other infrastructure that is very important for the overall well being of HIV infected children. This study is also not in

agreement with other similar studies from the same region.

## 5. SUMMARY OF THE THESIS

Our study was a cross-sectional study in which 70 HIV positive children attending the pediatric ART Clinic were enrolled and their proforma was filled which included the demographic data, details of HIV and drug regimen, their WHO stage, adherence percentage by pill counting method, CD4 count and viral load level.

- The mean age of the patient was  $12.57 \pm 3.31$  years, The youngest child was 5 years of age and the eldest was 18 years,. majority 57(81.4%) patients were in the age group of 10 to 18 years and 13(18.6%)cases were in the age group of 5 to 9 years.
- The majority of the 44(62.9%) children were males while 26(37%) cases were females.
- All the enrolled patients were on antiretroviral therapy.
- The mean age of diagnosis was  $8.13 \pm 3.89$  years including a minimum age of the patient was of 2years and a maximum of 16 years. Mean age of duration of HIV infection  $4.54 \pm 3.28$  years with including minimum age 6 months and a maximum of 12 years
- Mean duration of treatment was  $4.24 \pm 3.05$  years with a minimum duration of 6 months and maximum of 12 years
- Among 70 children 61(87.1%)patients had adherence more than 95% while 9 (12.9%) cases had adherence less than 95%.
- Among 9 nonadherent children, the main reason for nonadherence was that they forgot to take medicine in 8(88.9%) cases and 1 child (11.1%) was nonadherent because he did not like the medicine taste.
- Adherence was not related to age, sex, age at diagnosis duration of HIV infection, duration of treatment taken.
- Mean viral load in the adherent group was  $2379 \pm 5996.74$  copies per ml against  $46529.22 \pm 86633.12$ copies per ml in the non adherent group.
- THE mean CD4 count in the adherent group was  $794 \pm 281$  cells per cubic

millimeter against  $531 \pm 250$  cells per cubic millimeter in the nonadherent group.

- A viral load of  $<1000$  copies per ml was found in 28 (77.8%) cases in the adherent group and 1(11.1%) child in the nonadherent group. Viral load copies  $>1000$  copies per ml were found in 8(22.2%) subjects among the adherent group and 8(88.8%) subjects in the non adherent group.
- The adherent group was having significant virological suppression and also significantly higher CD4 count.

## 6. CONCLUSION AND RECOMMENDATIONS

This cross-sectional observational study was done to study the relationship between drug adherence and viral load in children living with HIV. We report that caregiver-reported adherence to ART done by pill counting among children attending our ART clinic is high. The majority of children reporting nonadherence by this method gave the reason that they forget to take medicine. The adherent group was found to have higher CD4 count and suppressed viral load. No relation of adherence to ART was found with age, sex, duration of HIV infection, duration of treatment taken.

## CONSENT AND ETHICAL APPROVAL

Written, informed consent was obtained from the children's caregivers and the ethics committee of Dr. Ram Manohar Lohia to grant permission for the study.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Akena D, Musisi S, Joska J, Stein D. The Association between Aids Related Stigma and Major Depressive Disorder among HIV-Positive Individuals in Uganda. *PLoS ONE*. 2012;7(11):e48671.
2. Stubbs BA, Micek MA, Pfeiffer JT, Montoya P, Gloyd S. Treatment partners and adherence to HAART in Central Mozambique. *AIDS Care*. 2009;21(11):1412–9.
3. Sethi AK, Celentano DD, Gange SJ, Moore RD, Gallant JE. Association between Adherence to Antiretroviral Therapy and Human Immunodeficiency Virus Drug Resistance. *Clin Infect Dis*. 2003;37(8):1112–8.
4. Simoni JM, Yard SS, Huh D. Prospective prediction of viral suppression and immune response nine months after ART initiation in Seattle, WA. *AIDS Care*. 2013;25(2):181–5.
5. Bello G, Simwaka B, Ndhlovu T, Salaniponi F, Hallett TB. Evidence for changes in behaviour leading to reductions in HIV prevalence in urban Malawi. *Sex Transm Infect*. 2011;87(4):296–300.
6. Bagenda A, Barlow-Mosha L, Bagenda D, Sakwa R, Fowler MG, Musoke PM. Adherence to tablet and liquid formulations of antiretroviral medication for paediatric HIV treatment at an urban clinic in Uganda. *Ann Trop Paediatr*. 2011;31(3):235–45.
7. Wachholz NIR, Ferreira J. Adherence to antiretroviral therapy in children: a study of prevalence and associated factors. *Cad Saude Pública*. 2007;23(suppl 3):S424–34.
8. Naco.gov.in; 2018. [Cited 6 September 2018]. Available:<http://naco.gov.in/sites/default/files/6%20Adherence%20counselling%20for%20children.pdf>.
9. Gortmaker SL, Hughes M, Cervia J, et al. Effect of combination therapy including protease inhibitors on mortality among children and adolescents infected with HIV-1. *N Engl J Med*. 2001; 345:1522–8.
10. Fogarty L, Roter D, Larson S, Burke J, Gillespie J, Levy R. Patient adherence to HIV medication regimens: a review of published and abstract reports. *Patient Educ Couns*. 2002;46:93–108.
11. Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med*. 2000;133:21–30.
12. Chesney MA, Morin M, Sherr L. Adherence to HIV combination therapy. *Soc Sci Med*. 2000;50(11):1599–605.
13. Murphy DA, Wilson CM, Durako SJ, Muenz LR, Belzer M. Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort in the USA. *AIDS Care*. 2001;13(1):27–40.
14. Reddington C, Cohen J, Baldillo A, Toyo M, Smith D, Kneut C, et al. Adherence to

- medication regimens among children with human immunodeficiency virus infection: *Pediatr Infect Dis J.* 2000;19(12):1148–53.
15. Williams PL, Storm D, Montepiedra G, Nichols S, Kammerer B, Sirois PA, et al. Predictors of Adherence to Antiretroviral Medications in Children and Adolescents With HIV Infection. *PEDIATRICS.* 2006;118(6):e1745–57
  16. Bhattacharya M, Dubey AP. Adherence to antiretroviral therapy and its correlates among HIV-infected children at an HIV clinic in New Delhi. *Ann Trop Paediatr.* 2011;31(4):331–7.
  17. Mehta K, Ekstrand ML, Heylen E, Sanjeeva GN, Shet A. Adherence to Antiretroviral Therapy Among Children Living with HIV in South India. *AIDS Behav.* 2016;20(5):1076–83.
  18. Martelli G, Antonucci R, Mukurasi A, Zepherine H, Nöstlinger C. Adherence to antiretroviral treatment among children and adolescents in Tanzania: Comparison between pill count and viral load outcomes in a rural context of Mwanza region. Chemin I, editor. *PLOS ONE.* 2019;14(3):e0214014.
  19. Seth A, Gupta R, Chandra J, Maheshwari A, Kumar P, Aneja S. Adherence to antiretroviral therapy and its determinants in children with HIV infection – Experience from Paediatric Centre of Excellence in HIV Care in North India. *AIDS Care.* 2014;26(7):865–71.

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