



## A STUDY TO DETERMINE EFFECT OF HAART (HIGHLY ACTIVE ANTIRETROVIRAL THERAPY) ON CSF VIRAL LOAD IN PATIENT WITH HIV INFECTION

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### ABSTRACT

**INTRODUCTION:** With the introduction of highly active antiretroviral therapy (HAART) there has been significant reduction in morbidity and mortality due to HIV infection which has now become a chronic disease. Another important aspect is effect of antiretroviral therapy on CSF HIV-1 RNA levels. **MATERIAL AND METHODS:** Twenty HIV positive patients with neurological manifestations and twenty patients of HIV without any neurological manifestation were enrolled. Detailed history regarding time and mode of detection of HIV infection and time of starting HAART was recorded. All patients underwent a detailed clinical examination with emphasis on neurological examination. Lumbar puncture was done and CSF examination was carried out in all forty patients (HIV patients with and without neurological manifestation). CSF was subjected to cytological, biochemical and bacteriological analysis and HIV viral load estimation. Simultaneously blood samples were collected from all patients for plasma viral load estimation. **RESULTS:** In our study all the cases (HIV/AIDS patients with Neuro AIDS) and controls (HIV/AIDS patients without Neuro manifestations) were males only. 45% of the cases and 60% of controls were in the age group of 25 to 35 yrs and 35 % of cases and 40% of controls were in age group of 36 to 45 yrs. Among cases (HIV patients with neurological manifestations), 60% were on HAART (>1 month) while among controls (HIV positive patients without any neurological manifestations, only 5% were on HAART (>1 month). **CONCLUSION:** CSF viral loads are much lower in HAART treated HIV positive patients with and without neurological manifestations as compared to treatment naive patients.

**KEYWORDS :** HAART, CSF HIV-1 RNA VIRAL LOAD, CD4 COUNT

### INTRODUCTION

With the introduction of highly active antiretroviral therapy (HAART) there has been significant reduction in morbidity and mortality due to HIV infection which has now become a chronic disease. Another important aspect is effect of antiretroviral therapy on CSF HIV-1 RNA levels. So far clinical utility of HIV-1 RNA detection in cerebrospinal fluid of patients on HAART has not been well defined [1]. HAART therapy can lead to decrease in HIV-1 RNA titres in plasma and CSF towards undetectable level [2]. Viral load dynamics in CSF and plasma may differ in both, untreated and those who have received antiviral therapy [3]. It has been reported that after initiation of ART, pattern of reduction in viral load in CSF and plasma may differ, which may be due to differences in capacity of different drugs to cross blood brain barrier, differences in initial susceptibility and subsequent development of drug resistant mutations in the two compartments. Moreover CSF RNA may correlate with plasma RNA only before development of AIDS and RNA levels in both compartments may become independent once AIDS develops [4]. Hence in HIV positive patients with neurological involvement, serial CSF viral load estimations may give a better prognostic indication regarding success of HAART in treating neuronal dysfunction [5].

### MATERIAL AND METHODS

**Design:** This was a prospective study conducted at a large tertiary care hospital for HIV patients. The study period was for three years. **Sample:** The current study included forty (40) patients (Twenty patient with neurological manifestations and twenty HIV positive patients clinically without any neurological manifestation). Ethical committee was consulted and approval was obtained. **Inclusion criteria:** Twenty patient of HIV infection with any neurological manifestation and twenty HIV/AIDS patients without any clinically apparent neurological manifestations. **Procedure:** Twenty HIV positive patients with neurological manifestations and twenty patients of HIV/AIDS without any neurological manifestation were enrolled in this study. All potential study subjects and controls were explained the nature of this study and enrolled thereafter with written consent. Detailed history regarding time and mode of detection of HIV infection and time of starting HAART was recorded. All patients underwent a detailed clinical examination with emphasis on neurological examination. Routine investigations of

HIV patients including CD<sup>4</sup> counts were carried out. In patients with neurological manifestation CT Scan Head was carried out where indicated. MRI, although envisaged initially, could not be done in all patients with neurological manifestations because of their poor general condition as they were deemed to be unfit to undergo MRI which requires patient cooperation. Thereafter lumbar puncture was done and CSF examination was carried out in all forty patients (HIV patients with and without neurological manifestation). CSF was subjected to cytological, biochemical and bacteriological analysis and HIV viral load estimation. Simultaneously blood samples were collected from all patients for plasma viral load estimation.

### RESULTS

#### TABLE -1AGE DISTRIBUTION OF PATIENTS WITH NEUROLOGICAL MANIFESTATIONS

Age Gp (Yrs)	Frequency of cases	Percentage
15-25 Yrs	2	10.00%
26-35 Yrs	9	45.00%
36-45 Yrs	7	35.00%
46-55 Yrs	2	10.00%

#### TABLE-2AGE DISTRIBUTION OF CONTROLS

Age Gp (Yrs)	Frequency of controls	Percentage
15-25 Yrs	0	0.00%
26-35 Yrs	12	60.00%
36-45 Yrs	8	40.00%
46-55 Yrs	0	0.00%

#### TABLE-3 DURATION OF HAART IN PATIENTS

Duration of HAART	Frequency of cases	Percentage
NO HAART	8	40.00%
1- 6 months	9	45.00%
6- 12 months	2	10.00%
>12 months	1	05.00%

#### TABLE-4 DURATION OF HAART IN CONTROLS

Duration of HAART	Frequency of controls	Percentage
No HAART	19	95.00%

<b>1- 6months</b>	1	05.00%
<b>6-12 months</b>	0	00.00%
<b>&gt;12 months</b>	0	00.00%

**TABLE-5 VIRAL LOADS IN PATIENTS & CONTROLS ON HAART & NOT ON HAART**

	Cases (HIV/AIDS patients with Neuro AIDS)		Controls (HIV/AIDS patients without Neuro AIDS)	
	On HAART (>1 months) (No 12)	Not on HAART (No 8)	On HAART (>1 months) No 1	Not on HAART No 19
<b>Mean Plasma Viral Load (copies/ml)</b>	24519.75	236792.3	44148	113493
<b>Mean CSF ViralLoad (copies/ml)</b>	2262.333	9697.25	0	502.4

**TABLE-6CSF VIRAL LOAD IN PATIENTS& CONTROL (HAART & TREATMENT NAIVE PATIENTS)**

CSF Viral Load Copies/ml	Patients		Controls on HAART	
	On HAART (>1 Month)	Not on HAART	HAART (>1 Month)	Not on HAART
<b>NIL (&lt;400)</b>	7 (58.33%)	0	1 (100%)	15 (78.95%)
<b>&gt;400</b>	5 (41.66%)	8 (100%)	0	4 (21.05%)
<b>Total</b>	12	8	1	19

**DISCUSSION**

In our present study we have tried to see the effect of HAART on the CSF viral loads in HIV infected patients as the declining titres can serve as a useful prognostic marker in patients who are undergoing successful antiretroviral therapy. In our study all the subjects were males. This is because of male patients are transferred from peripheral hospitals to immunodeficiency centre of BH Delhi Cantt,

Many of our HIV infected patients with neurological manifestations (60%) and one control (5%) had already received HAART for a period varying from one month to more than a year whereas 8 patients (40%) and 19 controls (95%) were treatment naive.

Mean CSF viral load in HIV infected patients with neurological manifestations was 5236.3 copies/ml while the controls had mean CSF viral load of **502.4 copies/ml**, thereby showing significantly higher viral load. Other factors associated with higher HIV-1 RNA levels were low CD4 count (<200cells/mm3) and detectable plasma HIV-1 [1]. Von Giesen et al found significantly higher CSF viral loads among patients with incipient minor motor defects and demented patients as compared to asymptomatic patient independent of antiretroviral therapy [6]. Similar observation has been made by Mellgren et al who observed significantly higher CSF viral loads both at baseline and after treatment in patients with neurological disease compared with neurologically asymptomatic patients [7].

Most of the reports in literature have shown decline in CSF RNA-1 levels with antiretroviral therapy. While total eradication of virus from body may not be possible, studies have shown that HAART leads to decline in HIV-1 RNA titre in plasma and CSF [8, 1, 2]. Short term effects of HAART on CSF HIV-1 RNA levels have been studied. Sharp reduction in CSF HIV RNA concentration was observed between 5 to 24 days after initiation of change in ART. There was rapid rise of HIV RNA in CSF and blood after interruption of ART [9]. Significant decline of viral load in CSF was observed with different regimens. HAART achieved 69% decline as compared to 0% decline in patients receiving one drug [10]. Decrease in CSF viral load with antiviral therapy was also observed by Saez-Lorens et al in a study of paediatric population [11]. Differences in CSF viral load were noted with different antiviral treatment regimens by Gisslen et al in a study of 79 patients [10]. In our study among the HAART treated HIV infected patients with neurological manifestations, mean CSF viral

load was 2262.33 copies/ml as compared to mean CSF viral load of 9697.25 copies/ml in treatment naive HIV positive patients. Whereas in controls (neurologically asymptomatic patients), treatment naive patients had higher mean CSF viral load (502.4 copies/ml) as compared to 0 copies/ml in patient who had received HAART for more than a month.

**CONCLUSION**

CSF viral loads are much lower in HAART treated HIV positive patients with and without neurological manifestations as compared to treatment naive patients.

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