ORIGINAL ARTICLE

PLASMA VIRAL LOAD, CD4 COUNT AND HIV ASSOCIATED DEMENTIA

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ABSTRACT

Background: Plasma viral load has proven valuable in predicting the future course of systemic HIV related disease and response to treatment.

Aim: In this study we have aimed to correlate plasma viral load and CD4 count with Mini Mental Status Examination (MMSE) scores and HIV Dementia Scales in patients diagnosed with HIV associated dementia (HAD).

Methodology: 69 subjects with HAD entered into the study and were assessed using MMSE and HIV Dementia Scale (HDS).

Results: A negative correlation was ascertained between plasma viral load and MMSE scores. No significant correlations were found between the scores on HDS and either plasma viral load or CD4 count.

Conclusions: This was one of the first studies on this issue from India and further studies in larger number of subjects are needed to form firm conclusions.

Key Words: HIV associated Dementia, Plasma viral load, CD4 count

INTRODUCTION

HIV infection is associated with a wide range of neurological manifestations with around 15-20% of patients developing progressive cognitive dysfunction known as HIV associated dementia (HAD).[1] The progression of HIV dementia is at a variable rate with cognitive, motor and behavioral symptoms all making their presence felt.[2] There is an increase in the prevalence of HAD worldwide due to anti-retroviral therapy. The therapy has enhanced the longevity of HIV patients with peripheral immunosuppression but dominance of HIV in the rain persists due to poor blood brain barrier permeability of these drugs leading to a gross increase in HAD.[3]

The exact neuropathogenesis of HAD is not understood. This is so despite the fact that 80% of patients show pathological changes in the brain including gliosis, neuronal loss and inflammation.[4-5] It has been proven that the central nervous system is a sanctuary for the persistence and replication of the HIV virus independent of peripheral HIV infection.[6] Researchers have tried to correlate the presence of HIV infected microglia to the severity of disease with inconclusive results.[7] There have been studies to elucidate the risk factors of HAD with injection drug use, female sex, older age and more constitutional symptoms prior to the onset of AIDS being some of the factors identified.[8-9]

Higher viral loads and lower CD4 counts are known to pose a greater risk for HAD. People are often at a greater risk when the CD4 count is less than 100-200.[10] A pivotal study quoted as a landmark proof in this area states that with a viral load > 30,000 the subject is at 8.5 times risk for dementia than when the viral load is > 500. CD4 counts of < 200 poses 3.5 times a risk for HAD compared to when the CD4 count is > 500.[11] Neurological dysfunction in HIV has been correlated to serum viral RNA while the same holds true for CSF viral RNA.[12]

There is a paucity of data in this regard from countries like India where HIV is ever increasing. The first case of HIV in India was reported in 1986 and presently there are 3.9 million people with HIV living in India.[13] In view of such a large problem the following study was undertaken with the aim to evaluate the clinical characteristics of patients with HAD and to correlate dementia to CD4 count and plasma viral load.

METHODOLOGY

The study was conducted on 69 patients with HAD who were following up in a private psychiatric clinic.

This diagnosis was made by the treating clinician using the HIV Dementia Scale (HDS) where a score of 10 or < 10 is significant and a detail neurological assessment is required. The scale has a specificity of 91% and a sensitivity of 80%. There are four measurable dimensions i.e. attention, psychomotor speed, memory and construction.[14] Cognitive impairment was further assessed using the Folstein Mini Mental Status Examination (MMSE) where the cut offs for age and educational level were applied.[15]

Patients of both sexes between the ages of 20-55 years were selected for the study. Patients with history of a general medical disorder, known neuropsychiatric conditions like head injury, opportunistic central nervous system HIV infections, seizures, persistent substance use disorders and history of psychotropic drug treatment during the past 3 months were excluded from the study to avoid patients having cognitive disturbances due to these causes. The patients were explained about the aims of the study and their confidentiality was assured. Informed valid written consent was obtained and the study was approved by a local research committee for ethical issues.

Demographic characteristics were assessed using a semi-structured proforma. Plasma viral load and CD4 count were assessed at the time of assessment. Correlation between CD4 count and MMSE scores as well as HDS scores and similar correlations for plasma viral load was performed using the Spearman rank correlation.

RESULTS

The study sample consisted of 58 males and 11 females. All subjects were educated upto secondary school or above. 87.93% males and 81.82% female subjects were married. All the female subjects were housewives. 70.69% of male subjects were employed. In 56.9% (33) males and 63.67% (7) female subjects diagnosed with HAD, only a year had elapsed since seropositivity. While in 37.93% (22) males and all remaining female subjects the duration since seropositivity was 1-5 years.

Table 1: Relationship of CD4 Count to MMSE and HDS Scores

Scores	Mean (SD)	r value
CD4 Count	265.66 (201.33)	
MMSE	26.3 (5.1)	0.0877
HDS – Attention	3.1 (1.2)	0.1555
HDS – Psyc. Speed	3.3 (1.3)	0.1342
HDS – Memory	3.06 (1.1)	0.1022
HDS – Construction	3.03 (1.05)	0.1235
HDS – Global	8.65 (4.11)	0.0433

When CD4 count was correlated to MMSE scores it was noted that as CD4 counts increase the MMSE scores would increase in parallel. When CD4 count was correlated to the items on the HDS, attention and memory deficits were more apparent with decreased CD4 counts. No correlation was found between psychomotor speed, construction and total HDS scores (table 1).

A negative correlation was found between plasma viral load and MMSE scores. No correlation was found between plasma viral load and other parameters on the HDS. Though psychomotor speed was correlated positively with viral load, it was not statistically significant (table 2).

Table 2: Relationship between Plasma Viral Load, MMSE & HDS Scores

Scores	Mean (SD)	r value
Plasma Viral Load	110862 (65221)	
MMSE	26.3 (5.1)	- 0.131
HDS – Attention	3.1 (1.2)	- 0.0009
HDS – Psyc. Speed	3.3 (1.3)	0.1665
HDS - Memory	3.06 (1.1)	- 0.054
HDS – Construction	3.03 (1.05)	0.1567
HDS - Global	8.65 (4.11)	0.1533

DISCUSSION

Investigators have shown that plasma viral load predicts the rate of decrease of CD4 count, progression of HAD and progression to AIDS and death. The combined measurement of CD4 count and plasma or CSF viral load is better indicator of progression and prognosis.[16] A higher plasma viral load may also probably indicate a large number of circulating HIV infected monocytes that could enter the brain and establish early CNS infection trigger mechanisms that cause neuronal injury.[17]

Though CSF viral load may have been ideal, plasma viral load was assessed in the study due to easy accessibility and the fact that studies have proven the significant relationship between CSF and plasma viral load. It is worth noting that both plasma and CSF viral load are not equivalent to the actual brain viral load.[18]

We believe that plasma viral load over the course of the illness may correlate with degree of CNS dysfunction and progression of HAD. It is well known that viral load increases in the later stages in AIDS where HAD may set in and this may be detected in plasma.[18]

We noted in the study that as CD4 count increased MMSE scores increased in parallel. It probably could be interpreted that HAD is less likely in patients with a higher CD4 count. Similar effects are also seen with elevation of CD4 counts after anti-retroviral therapy.[19]

We found a negative correlation between plasma viral load and MMSE scores indicating that increased viral load is associated with a severe degree of dementia. Though viral load did not correlate significantly with any of the parameters on the HDS including global scores, we probably assume that due to early stages of dementia, the symptoms may have been subtle and hence not statistically significant. Later, probably a

global dementia with memory loss and language impairment would ensue even leading to vegetative states.[19]

CONCLUSIONS

This is one of the few studies on this topic from India. Relatively little is known about the relationship between plasma viral load, HAD and neurological manifestations of HIV with few studies being done in the region. We tried to achieve a relationship between plasma viral load, CD4 count and HAD. Further larger studies across diverse groups are needed to establish these relationships in a concrete manner.

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