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# Genetic Variations of V3 and C3 regions in gp120 protein of HIV-1 env gene

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## Abstract

**Background:** HIV-associated neurocognitive disorder (HAND) is an important cause of morbidity of HIV patients. The development of neurological disease among individuals having an HIV infection is variable. The env sequences of HIV-1 are important for cell entry and neurotropism. The env sequences vary among individuals having HIV infection. Hence the development of neurotoxicity differs among individuals with HIV infection. So far, none of the studies reported the mechanism of neurotoxicity in astrocytes. Hence we comprehended the genetic profile of the gp120 protein of HIV-1 env gene which influences the pathogenesis of neurocognitive diseases

**Method:** We led the search utilizing multiple databases, specifically, EMBASE, PubMed (Medline), and Google Scholar.

**Description:** Pathogenesis of HAND is influenced by HIV-1 env sequences. The gp120 glycoprotein serves as a determinant to cross the blood-brain barrier and maintain neurocognitive impairments. The persistence of env sequences within the CNS leads to neurovirulent features and neurotoxicity. The evolution of the env gene is a continuing process that contributes to neurocognitive disease severity.

**Conclusion:** Genetic profiling of V3 and C3 regions of gp120 motifs in a larger number of HAND patients with various ethnic groups will provide data for the correlation of V3 and C3 regions with IHDS and cognition parameters. This will help to define the risk factor which can contribute to neurocognitive disease.

**Keywords:** HAND; HIV; V3 and C3 regions; env sequences; neurotoxicity in HIV patients

## Introduction

HIV-associated neurocognitive disorder is now acknowledged as a cause of morbidity and mortality among HIV-infected individuals [1]. Mostly, it occurs when CD4+ lymphocyte counts fall below 200 cells/mL and late stages of acquired immunodeficiency syndrome (AIDS) [2]. Nearly 50% patients manifest the symptoms of HAND prior to their deaths [3]. The prevalence of HAND in adult people ranges from 19% to 52% in developed country [4-5], and 14% to 64% in developing countries [6-7]. In India, the prevalence of HAND patients is ~ 32.50% [8].

The multifactorial disease like HAND is influenced by continuous immune activation and central nervous system (CNS) inflammation [9]. The development of HAND is influenced by many other factors like host and HIV-related which speed up the progression of HAND [10-13]. HAND and the neurotoxicity is result of synchronised actions of trans-activating protein (Tat) and envelope glycoprotein (Env) [14]. It was reported that gp120 fragment of Env protein could mediate neuronal damage in brain tissue [15-17]. The genotypic and phenotypic diversity of HIV is influenced by hypervariable region 3 (V3) of gp120 fragment. The viral phenotypes and cell tropism are influenced by the interaction of V3 (V3 loop) with chemokine co receptors CCR5 or CXCR4 [18]. The persistent replication of virus in the CNS has been associated with CCR5 tropism, macrophage/microglia tropism [19-21]. The viral diversity in the CNS resulted from the inability of serum to neutralize recombinant virus containing C2V3 regions [22]. Evidence indicates, variation in V3 region influences CNS toxicity [23-24]. A study reported significant genetic differences for constant region 4 (C4 region) while compared in the samples of CSF and plasma between patients with and without HAND [25]. The amino acid composition and PNLGs spanning of C4 to V5 have a roles in antibody evasion [26] and enhanced viral infectivity [27-28, 25].

Hence, diversity in env gene sequence of CNS may provide persistence of higher virus infection in the CNS. Till now, the exact time of advancement of env in the CNS is not known. Although studies suggested that appearance of diverse viral population consequences before the manifestation of neuropath logical condition [29-31]. The evolutionary patterns of viral isolates in tissues vary between patients with or without HAND [32, 25]. In HAND patients, a higher rate of genetic evolution was observed in the lymphoid tissues [25]. A study reported a higher viral diversity in patients with HAD than without HAD [22].

Worldwide, ~50% of the HIV infection is associated with the subtype C (Esparza et al., 2000). It is rapidly growing epidemics in Asia and sub-Saharan Africa including China and India [33]. In addition to that the progression of HIV infection is influenced by virus subtype, genetic, demographic factors [34-35]. The molecular and biological properties of subtype C vary from other subtypes. Till now, report has not been published whether these differences explain to differential pathogenic properties [36]. Hence we comprehended the genetic profile of the gp120 protein of HIV-1 env gene which influences the pathogenesis of neurocognitive diseases

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## Method

We led the search utilizing multiple databases, specifically, EMBASE, PubMed (Medline), and Google Scholar. We have done the literature survey on HIV-1 env gene sequence.

## Discussion

Mostly neurotoxicity is determined by cysteine-rich motifs of Tat in clade C isolates. In addition to that, variability in neurotoxicity is influenced by genetic differences in gp120 of clade C [37]. In Tat sequence analysis, it was reported that there are six amino acid residues which are differentially conserved in subtype C Tat (C-Tat). Out of that, more than 90% are subtype C viruses encoded a serine and >99% are conserved in non-subtype C viruses encoded a cysteine (at position 31) [38]. In addition to that, the neurotoxicity is influenced by clade-specific variations [39]. It was reported that HIV clade C strains of India is less neurotoxic than clade C strain from southern Africa [39]. Individuals with clade B HIV-1 infection are more susceptible to neurotoxicity than clade C [40]. However, none of the study described the mechanism of neurotoxicity in astrocytes [41]. The mediators of neurotoxicity are present in the V3 and C3 regions of gp120 motifs. Variation in env sequence not only affects the cell entry and neurotropism but also affects the neurotoxicity. Though, the specific factors which contribute to development of neurotropic and neurovirulent is not well defined.

## Summary

Pathogenesis of HAND is influenced by HIV-1 env sequences. The gp120 glycoprotein serves as a factor to cross the blood-brain barrier and conserve neurocognitive impairments. The variation in env gene sequences in the CNS leads to neurotoxic and neurovirulent features.

## Future

Further analysis of the HIV-1 env gene sequence in larger number of HAND patients will address the genetic variations of gp120 protein of HIV-1 env. Comparative studies on genetic profiling of V3 and C3 regions of gp120 motifs among HAND patients of different ethnic region will provide correlation between V3 and C3 regions and IHDS and cognition parameters.

## Conclusion

Comparative studies on genetic profile of V3 and C3 regions of gp120 protein will be helpful to address the pathogenesis of HAND patients. Correlation of genetic profile of V3 and C3 regions of gp120 motifs with International HIV Dementia Scale (IHDS) and cognition parameters (attention, memory, language, reaction time, and perception) will provide viral marker for the development of HAND

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