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Cognitive Decline in People Living with HIV in India and Correlation with Neurometabolites Using 3T Magnetic Resonance Spectroscopy (MRS): A Cross-Sectional Study

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Abstract : Introduction: A significant number of patients having human immunodeficiency virus (HIV) infection show a neurocognitive decline (NCD) ranging from minor cognitive impairment to severe dementia. The possible causes of NCD in HIV-infected patients include brain injury by HIV before cART, neurotoxic viral proteins and metabolic abnormalities. In the present study, we compared the level of NCD in asymptomatic HIV-infected patients with changes in brain metabolites measured by using magnetic resonance spectroscopy (MRS). Methods: 43 HIV-positive patients (30 males and 13 females) coming to ART center of the hospital and HIV-seronegative healthy subjects were recruited for the study. All the participants completed MRI and MRS examination, detailed clinical assessments and a battery of neuropsychological tests. All the MR investigations were carried out at 3.0T MRI scanner (Ingenia/Achieva, Philips, Netherlands). MRI examination protocol included the acquisition of T2-weighted imaging in axial, coronal and sagittal planes, T1-weighted, FLAIR, and DWI images in the axial plane. Patients who showed any apparent lesion on MRI were excluded from the study. T2-weighted images in three orthogonal planes were used to localize the voxel in left frontal lobe white matter (FWM) and left basal ganglia (BG) for single voxel MRS. Single voxel MRS spectra were acquired with a point resolved spectroscopy (PRESS) localization pulse sequence at an echo time (TE) of 35 ms and a repetition time (TR) of 2000 ms with 64 or 128 scans. Automated preprocessing and determination of absolute concentrations of metabolites were estimated using LCModel by water scaling method and the Cramer-Rao lower bounds for all metabolites analyzed in the study were below 15\%. Levels of total N-acetyl aspartate (tNAA), total choline (tCho), glutamate + glutamine (Glx), total creatine (tCr), were measured. Cognition was tested using a battery of tests validated for Indian population. The cognitive domains tested were the memory, attention-information processing, abstraction-executive, simple and complex perceptual motor skills. Z-scores normalized according to age, sex and education standard were used to calculate dysfunction in these individual domains. The NCD was defined as dysfunction with Z-score ≤ 2 in at least two domains. One-way ANOVA was used to compare the difference in brain metabolites between the patients and healthy subjects. Results: NCD was found in 23 (53%) patients. There was no significant difference in age, CD4 count and viral load between the two groups. Maximum impairment was found in the domains of memory and simple motor skills i.e., 19/43 (44%). The prevalence of deficit in attention-information processing, complex perceptual motor skills and abstraction-executive function was 37%, 35%, 33% respectively. Subjects with NCD had a higher level of Glutamate in the Frontal region (8.03 ± 2.30 v/s. 10.26 ± 5.24, p-value 0.001). Conclusion: Among newly diagnosed, ART-naïve retroviral disease patients from India, cognitive decline was found in 53\% patients using tests validated for this population. Those with neurocognitive decline had a significantly higher level of Glutamate in the left frontal region. There was no significant difference in age, CD4 count and viral load at initiation of ART between the two groups.

Keywords : HIV, neurocognitive decline, neurometabolites, magnetic resonance spectroscopy
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