Analysis of CAG Repeats in HTT Gene Among Huntington 's Disease (HD) Patients and Normal Population of a Sri Lankan Cohort

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Introduction: CAG repeat length in normal chromosomes is lower in countries with low HD prevalence compared to West. Neuropathological studies suggest that the pathogenic HD gain of function could be the formation of ubiquitinated aggregates of the mutated huntingtin protein.

Method: Clinically diagnosed HD patients [n=18; Male- 5 (28%), Female- 13 (72%); age at onset 15-64; mean 42±13.8yrs] from three tertiary hospitals were studied. Sociodemographic factors and clinical data were obtained using a standard questionnaire. Patients were subjected to CAG repeat analysis along with age matched controls (n=9).

Results: Patients [Adult onset n=17 (94%), Juvenile onset n=1 (6%)], Familial inheritance n=15, 83%. The mean CAG length on normal chromosomes in controls 17.1±1.5, Patients normal allele 19±2.6, abnormal allele 46.7±7. An inverse correlation observed between the age onset and the CAG repeat length of abnormal allele r=0.5993 P<0.001. The ranges for Total Motor Score; 14-93 (mean- 46±20), Functional Score; 0- 25 (mean- 15.7±6), Mini Mental Status Examination; 13- 26 (mean- 20±4) where UHDRS Motor Score P<0.001 and MMSE P<0.01 significantly correlate with disease duration.

Conclusions: The lower epidemiology in Sri Lankans can be partly explained by the less CAG repeats even though there may be variation across ethnic groups. We intended perform neuropathological analysis to correlate neuropathological severity with CAG repeat length and to evaluate the neuroprotective effect of dietary phytochemicals on aggregated mutated protein in brain utilizing the established Brain Bank.