ABSTRACT

Polyomaviruses are potentially oncogenic viruses found in humans, in other mammals and birds all over the world. JC polyomavirus (JCPyV) is widespread human virus with profound pathogenic potential. It remains latent, predominantly within epithelial tissues, and does not cause any disease or symptoms in the immunocompetent individuals. However, in immunocompromised individuals, JCPyV has been shown to cause progressive multifocal leucoencephalopathy (PML) in addition to suspected tumourigenesis in human central nervous system.

There is a resurgence of interest in the study of occurrence, genotype and pathogenic associations of human Polyomaviruses in recent years, especially after wide spread transmission of HIV. In the present study, we have ascertained the presence of JCPyV in urine, blood and CSF samples from individuals of sub-Himalayan part of West Bengal State of India. Two groups were considered in the present study, one group containing immunocompromised individuals and the other group consisting of non-immuncompromised subjects. Six hundred thirteen (613) samples were collected from different individuals during the study with their prior consent. An overall incidence of 8.15% was observed in this region based on polymerase chain reaction (PCR) analyses, and these results were further confirmed by sequencing of PCR products. The incidence rate of JCPyV in the immunocompromised group i.e., 10.60% was higher than that in the non-immunocompromised group (6.30%). Prevalence of JCPyV has been recorded in some of the tribal populations of this region showing variations in the incidence of the virus. About 3.76% of individuals from Oraon and Munda tribes, 12.62% of individuals

from Rabha tribe and 5.55% of individuals from Mech tribal group showed presence of JCPyV in body fluids.

The prevalent genotypes of these natural isolates have also been characterized in this study. Pairwise sequence comparison and alignment of the Non-coding Control Region (NCCR) sequences of these strains appeared to be comparable and related to the archetypal JCPyV (CY) and the Tibetan LH3 strains, however with some alterations in few key positions. A 10-nucleotide (169-178) deletion in the block B and one di-nucleotide (454-455) deletion in block F were observed in the isolates. Point mutations in seven different sites within the NCCRs of the endemic strains were recorded when compared with the archetype strain CY. The sequence analyses were done with regard to transcription-factor binding to DNA sequence elements of endemic JCPyV NCCRs. Two prominent features within the endemic JCPyV NCCR Box B were the absence of full-length Purα/YB-1 binding site and the presence of Sp1 binding site in the same region. A di-nucleotide deletion was found within the p53 binding site of endemic JCPyV strains from the Oraon/Munda group as well as NCCR sequences of pregnant women but was absent from the isolates of Rabha tribe NCCR sequence.

Pairwise comparison and phylogenetic analyses based on VP1 and large T-antigen sequence revealed that the endemic JCPyV isolates from Rabha tribes had maximum similarity with the European type of JCPyV strain i.e., Type 1B, and the isolates from the Oraon and Munda tribes were almost identical to the Type 2D strain. Type 2D is the Indian subtype and is prevalent mainly in Asians and South Asians.

JCPyV DNA load in individuals of this region was also quantified. Real-time PCR was performed using SYBR green dye to undertake absolute quantification of

JCPyV load in blood and urine samples. A wide range of viral load was found in the samples ranging from 3.52×10^2 to 6.71×10^6 copies/ml of sample. The mean viral DNA load in urine samples was found to be higher than that in the blood samples. The mean (1.28×10^6) and the median (9.47×10^5) viral copy number recorded in the present study are comparatively higher than in some of the earlier reported studies. However, more studies may be required to substantiate these claims.