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Pathological and molecular studies on Coxsackie virus a-16 (cva-16) isolated from hand, foot and mouth disease (HFMD) in India, using neonatal mice model

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Coxsackie virus A-16 CVA-16 is one of the major etiological agents to cause hand, foot and mouth disease, among children. Severity of the disease might cause clinical manifestations leading to the neuronal involvement. Studies conducted earlier in India revealed circulation of CVA-16 as a major *Enterovirus* (EV) type associated. Despite, no attempts have been made to understand the mechanism of pathogenesis of CVA-16 strains isolated from HFMD. The present study highlights the pathogenesis and molecular aspects of CVA-16 strains isolated from HFMD cases using neonatal mice model. ICR mice were inoculated with CVA16/311 virus by intra-peritoneal route (I.P.) and were harvested at different time-points. Histopathological evaluation, CVA-16 specific antigen detection, viral kinetics using complete VP1 gene amplification of different organ tissues, nucleotide sequencing and phylogenetic analysis was carried out. CVA-16/311 infected mice showed clinical symptoms of weight loss, difficulty in movement, hind limb paralysis on day 5 of P.I.D. Hind limb muscles showed severe necrosis, dissolution of muscle fiber cells, infiltration of inflammatory cells and neuronal degeneration in brain. High level expression of CVA-16/311 viral antigen in limb muscles, brain and heart was observed. Viral kinetics studies revealed presence of CVA16/311 sequences in the organ tissues from day 5-7 of P.I.D. Phylogenetic analysis of full *VP1* gene showed presence of B1c sub-genotype. To the best of knowledge, such study is reported for the first time from India.

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