

## ABSTRACT

Human adenoviruses (HAdVs) are common pathogens associated with diseases affecting the respiratory tract, gastro-intestinal tract as well as various organs like the liver, kidney and the brain. Currently there are 60 human adenovirus serotypes classified into 7 species A to G on the basis of serology, genome sequencing and phylogenomics. HAdV species B, C and E are mainly implicated in respiratory tract infections whereas the other species are associated with gastro-intestinal, genitourinary, and ocular infections. The respiratory HAdV species play a significant role in pediatric infections accounting for 10% of overall respiratory illnesses and 5%–11% of pneumonia cases. The burden of diseases due to respiratory adenoviruses in Kenya has not been studied. There is no documented data on respiratory human adenovirus species and serotypes circulating in the country.

The aim of this study was to characterize respiratory human adenoviruses using serological and molecular approaches. Specifically the study sought to determine the species and serotypes of HAdVs that were associated with pediatric respiratory infections in New Nyanza Provincial General Hospital in the period of June 2010 to June 2012.

HAdVs were isolated from 16 archived nasopharyngeal swab patient specimens after inoculation into cultured Hep2 cells. After cytopathic effect observation, presence of adenovirus was confirmed through immunofluorescence assay. Virus DNA was extracted from the isolates followed by PCR amplification of the hyper-variable region 7 located in loop 2 region of hexon gene. The amplicons were sequenced using the Sanger dideoxy termination method followed by bioinformatics analyses of the nucleotide sequences. The hexon nucleotides sequences were used to classify the HAdV isolates into various species and serotypes by use of phylogenomics.

Nucleotide sequences of hexon loop-2 fragment of approximately 500 base pairs were obtained. Multiple sequence alignment of the loop-2 sequences with reference sequences obtained from other parts of the world revealed the location of the hyper-variable region at 1330-1400bp; a region characterized by several nucleotide substitutions, insertions and deletions. Phylogenomics analysis showed that during the study period, respiratory HAdV species B and C were associated with respiratory infections among pediatric patients attending New Nyanza Provincial General Hospital accounting for approximately 1% of the overall respiratory viruses. There were no cases of infections caused by respiratory HAdV E implying that this species was not in circulation during the study period. HAdV C was the predominant species accounting for 68.75% of the reported cases with serotype distribution as HAdV C1-25%, HAdV C2-25%, HAdV C5-6.25%, and HAdV C6-12.5%. HAdV B serotype 7 was the most prevalent serotype at 31.25%. HAdV C5 and HAdV B7 sequences were found to be under positive selection pressure indicating that these viruses are undergoing an evolutionary process which signifies instability in their genomes. Characterization of respiratory human adenoviruses that circulated at New Nyanza Provincial General hospital during the study period revealed that species B and C were present but not E. There was significant genetic variation in the hexon gene of the HAdVs seen at this site compared to those from other parts of the world implying continuing evolution of respiratory HAdVs. To gain a complete understanding of this evolutionary process, whole genome sequencing of these viruses is called for in order to determine genetic stability and uniqueness of these viruses.