RESEARCH PAPER | Medical Science | Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

Human Adenovirus in Hospitalised Children at a Tertiary Care Center in Jaipur

KEYWORDS: Human Adenovirus, acute respiratory infection, Children ≤ 5 years of age.

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ABSTRACT

Background: *Human Adenovirus (HAdV) causes Acute Respiratory Infections (ARIs) with significant mortality and morbidity in infants and Children.*

Aim: *To determine the occurrence of HAdV in hospitalised children of age ≤ 5 years.*

Materials and Methods: *Sterile viral transport media was used for the collection of throat swabs and nasopharyngeal aspirates from children with ARI. Viral nucleic acid was extracted by using automated nucleic acid extractor (Biomeuriex). Real time RT-PCR was done by using HAdV specific primer probe on ABI 7500 Fast Dx (Life Technologies, USA)*

Results: *The total positivity for HAdV was found to be 25/225 (11.11%). Among the total positive samples males were predominantly infected with HAdV in 20/25(80.0%) than females in 5/25(20.0%). Human Adenovirus was predominant in the age group of 1-12 months (84.0%). HAdV positive patients presented with cough in 25/25(100.0%), fever in 24/25(96.0%), and pneumonia in 8/25(32.0%). Highest peak of HAdV was observed in the month of February 2014.*

Conclusion: *HAdV was associated with 11.11% of hospitalised children with ARI. 32.0% of HAdV positive patients had pneumonia. Adenovirus should be tested in children with ARI. Unnecessary use of antibiotics can be prevented by timely detection of HAdV.*

Introduction:

Human *Adenovirus* (HAdV) causes respiratory illness which can be upper or lower respiratory infection and accounts 5-15 % in hospitalised infants and children for respiratory infection (1, 2). HAdV is responsible for 3-5% of lower respiratory tract infections in infants and children worldwide. Frequency of Acute Lower Respiratory Tract Infection (ALRI) with HAdV is low but it causes severe outcomes (3**)**. The virus can cause institutional out breaks and sporadic infections. HAdV causes severe disease in newborns and immunocompromised children, but can rarely cause serious and fatal illness in healthy children (4**).** Clinical signs and symptoms of HAdV infection are variable and non specific (2). HAdV associated pneumonia is serious sequelae requiring hospitalisation in children less than 2 years of age (5).

Based on the HAdV type, the epidemiological characteristics vary. The virus is transmitted by direct contact, faeco-oraly and rarely due to water born transmission. Infecting site of the body may vary depending on HAdV species. HAdV B and C species serotypes are mostly associated with Acute Respiratory Disease (ARD) (6).

The virus circulation occurs round the year and is indistinguishable from other respiratory viral infection (7). Cell culture is very sensitive technique for the isolation of HAdV but has limited clinical utility since it takes several days (1). Modern molecular technique, polymerase chain reaction (PCR) is a sensitive, specific and rapid technique as compared to traditional cell cultures, immunofluorescence (IF), and serology (5). To date there is no drug or vaccine available for the treatment of HAdV infections. The present study was undertaken to detect the occurrence of HAdV in hospitalised children ≤ 5 years of age with ARI.

Methodology:

Study setting:

This was a prospective study done at ICMR Grade-I Virology Laboratory -Advance Basic Science and Clinical Research Laboratory, Department of Microbiology & Immunology, Sawai Man Singh Medical College, Jaipur from January 2014 to August 2014.

Sample size calculation:

The sample size calculation was done by using the formula $n = 4\ pq/l^2$. (where n = total number of samples; 4 is the factor to achieve the confidence level of 95%; p = known prevalence; q = 100 – p, and l = allowable permissible absolute error, set at 4%). The sample size calculated was 163 with a prevalence rate of 7% for ARI in children as reported by National Family Health Survey – 3.

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Patients:
The patients were of ≤ 5 years of age. The clinical signs and symptoms observed include fever, cough, sore throat, nasal catarrh, shortness of breath, pneumonia, bronchiolitis and wheezing. All the children were hospitalised.

Sample collection and transportation:
Sterile viral transport media was used for the collection of throat swabs and nasopharyngeal aspirates from children with ARI. Following collection of samples and labelling, transportation of samples was done at the earliest to the laboratory on ice. Informed consent was obtained from the parents / guardians of the subjects. The study was approved by institutional ethics committee.

Nucleic Acid extraction:
Extraction of viral nucleic acid was done by using EasyMAG automated nucleic acid extractor (Biomeuriex) as per manufacturer's instructions. 110 µl of viral nucleic acid was extracted in the final step from a sample volume of 400 µl.

PCR:
Real time RT-PCR was performed for the detection of HAdV on ABI 7500 Fast Dx (Life Technologies, USA) thermocycler by using Human *Adenovirus* specific primer probe as described earlier (8).

Results:
Age-wise distribution of Patients:
All the samples were collected from hospitalised patients and the subjects enrolled in the study were between 1-60 months of age. The distribution of the subjects as per age was as follows; highest in 1-12 months 165(73.33%), followed by 13-24 months 33(14.67%), 49-60 months 15(6.66%), 25-36 months 11(4.88%), 37-48 months 1(0.44%) (Table-1).

Table-1: Age-wise distribution of patients enrolled in the study

Age in months	Total number of samples tested
1-12	165/225 (73.33%)
13-24	33/225 (14.67%)
25-36	11/225 (4.88%)
37-48	1/225 (0.44%)
49-60	15/225 (6.66%)
Total	225 (100%)

Month wise collection of samples:
Details of samples collected as per age, months are given in Table 2 where the highest numbers of samples were collected during winter months.

Table-2: Month-wise distribution of samples enrolled in the study from January 2014 - August 2014

Month/Year	1-12 months	13-24 months	25-36 months	37-48 months	49-60 months	Total Samples
January 2014	45	9	2	-	3	59
February 2014	42	2	-	-	-	44
March 2014	17	8	1	-	1	27
April 2014	16	6	2	1	3	28
May 2014	15	2	-	-	5	22
June 2014	13	3	1	-	1	18
July 2014	12	2	3	-	1	18
August 2014	5	1	2	-	1	9
Total	165	33	11	1	15	225

Distribution of HAdV:
A total of 225 samples from hospitalised children of age ≤ 5 years were tested for Human *Adenovirus* infection. Out of which, 175 (77.78%) were of males and 50 (22.22%) were of females. The total positivity for HAdV was found to be 25/225 (11.11%). Among the total positive samples males were predominantly infected with HAdV in 20/25(80.0%) than females in 5/25(20.0%) (Figure-1).

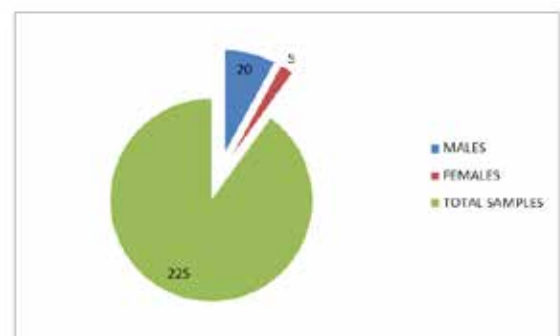

Figure-1: positivity of Human Adenovirus in Males and Females

HAdV among different age groups:
Human *Adenovirus* was predominant in the age group of 1-12 months (84.0%) followed by 13- 24 months age group (8.0%). HAdV was not detected in the age group 37-48 months (Figure-2).

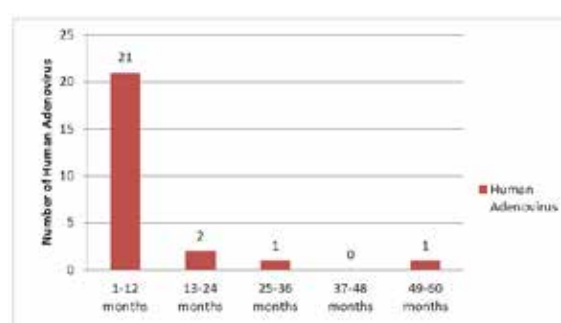

Figure-2: Age-wise distribution of Human Adenovirus in children ≤ 5 year

Association of HAdV with different signs & symptoms:
Human *Adenovirus* positive patients presented with cough in 25/25(100.0%), fever in 24/25(96.0%), shortness of breath in 17/25(68.0%), pneumonia in 8/25(32.0%) (Table-3).

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Table-3: Positivity of Human Adenovirus in relation to different signs & symptoms

Signs & symptoms	Human Adenovirus
Cough	25/25(100.0%)
Fever	24/25(96.0%)
Shortness of breath	17/25(68.0%)
Pneumonia	8/25(32.0%)
Bronchiolitis	2/25(8.0%)
Wheezing	0/25(0.0%)
Sore throat	0/25(0.0%)
Nasal catarrh	0/25(0.0%)

Month-wise distribution of HAdV:
During the study period of eight months starting from January 2014 to August 2014 HAdV was distributed in all the months except in March 2014. Highest peak of HAdV observed in the month of February 2014. The second best peak was observed in the months of January and June 2014. The overall distribution of HAdV was found to be more in winter months as compared to other seasons (Figure-3)

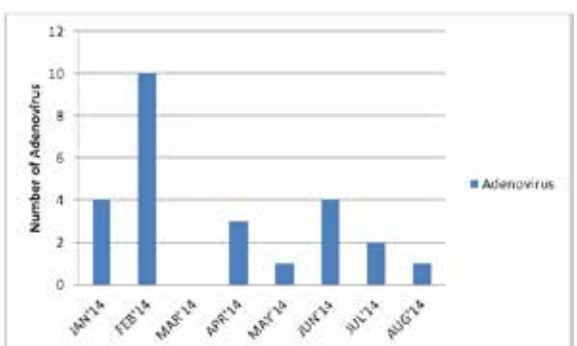

Figure-3: Distribution of Human Adenovirus from January 2014 - August 2014

Discussion:
The present study was conducted at a tertiary care centre in Jaipur to study the occurrence of HAdV in hospitalised children aged ≤ 5 years from January 2014 - August 2014 for a period of 8 months. HAdV is an important pathogen associated with ALRI resulting in death even in healthy children (9). Our study reported a positivity of 11.11% for HAdV in hospitalised children with ARI. This observation is lower when compared to an earlier study from Brazil which reported a positivity of 15.8% in children with ALRI. A previous study from Taiwan reported a positivity of HAdV as high as 83.5% in children with respiratory tract infections (5). However the techniques employed and study period may vary in different studies.

The positivity of HAdV in the present study was found to be predominant in children up to 2 years of age as compared to children > 2 years of age. This finding is similar to an earlier study from Philippines (9). Children with younger age group are likely to prone for HAdV associated disease (5).

Present study reported positivity of HAdV based on the signs and symptoms presented by the children at the time of admission to the hospital. Among the total HAdV positive samples, cough and fever were the most predominant clinical symptoms observed. Cough was reported in 25/25(100.0%), fever in 24/25(96.0%), pneumonia in 8/25(32.0%) and bronchiolitis in 2/25(8.0%) of hospitalised children. Earlier study from Iran (2) reported fever in 97.2%, Argentina (10) reported cough in 87.4%, Rome (11) reported pneumonia in 31.2.0% and bronchiolitis in 10.3%, of children with HAdV positivity.

Our study reported predominance of HAdV in male children as compared to females. This is similar with an earlier study from China (3). HAdV was found to be circulating during all the moths in our study with exception to March 2014. However the pattern of circulation varied during different months in the present study with its peak activity in the months of winter. Highest number of positive cases were observed in the month of February 2014. Circulation of HAdV without specific seasonality was also observed in a previous study from Utah (1) but the pattern of circulation of HAdV of the present study varied with the study from Utah (1). The seasonal activity of HAdV varies with different geographical locations, climatic conditions and the genetic makeup of individuals.

The present study was conducted only on hospitalised children. Further species identification and serotyping of HAdV was not done in our study. Species identification and serotyping may help to provide better understanding about the activity and epidemiology of HAdV in our area.

Conclusion:
Our study reported a significant positivity of 11.11% for HAdV in hospitalised children ≤ 5 years of age and significant number of these patients (32.0%) had pneumonia. Early detection of HAdV can help in proper management of patients and help avoid misuse of antibiotics. Since there is no antiviral and vaccine for HAdV, proper preventive measure may reduce the disease burden in children. Studies based on large number of samples from other parts of Rajasthan are required to better understand the occurrence of HAdV in children and for planning of public health strategies.

Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

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