International Journal of Contemporary Pediatrics
Darisetty S et al. Int J Contemp Pediatr. 2025 Jul;12(7):1120-1124
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20251863

Original Research Article

Prevalence of adeno virus associated diseases among pediatric population in a tertiary care teaching hospital

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Received: 29 April 2025
Accepted: 04 June 2025

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ABSTRACT

Background: Human adenoviruses (HAdV), can cause infections at any age but most commonly in young children and infants. Most children have experienced at least one bout of adenovirus infection by ten years old.
Methods: A prospective observational study was conducted during July 2023 to December 2023 with 100 patients. Clinical data was collected from patients diagnosed with adenovirus to study adenoviral associated diseases, clinical manifestations and treatments administered. Statistical analysis was done using statistical package for the social sciences (SPSS) version 26.0, $p<0.05$ was considered significant.
Results: In the current study children are between 1 month to 15 years and males (55%) outnumber females (45%). The most prevalent symptoms were high-grade persistent fever (100%), cough (79%), cold (67%), vomiting's (34%), shortness of breath (18%) abdominal pain and noisy breathing (12%), sore throat (10%), headache (5%), conjunctivitis (3%) and ear pain (1%). Comorbidities were, gastroenteritis with dehydration (3%), enlarged adenoids (5%), enlarged tonsils (4%), sepsis (4%), sickle thalassemia (1%), pansinusitis (1%) and shock with down syndrome (1%). Support received include, nebulization (69%), high-flow nasal cannula (HNFC) (2%), oxygen (2%), both HNFC and oxygen (1%). 48% received azithromycin, of which on day of admission (12%), second day (14%), third day (13%), fourth day (9%). Notably all children were discharged successfully without encountering any complications.
Conclusions: HAdV infections are commonly associated with high-grade fever, challenging the conventional perception that respiratory infections are their predominant manifestation. Timely, precise detection of HAdV infection is essential for enhancing treatment and reducing inappropriate use of antibiotics.

Keywords: Human adenovirus, Epidemiology, Clinical manifestations

INTRODUCTION

Human adenovirus infections can lead to a variety of illnesses in individuals with a competent immune system, typically presenting as mild and self-limiting conditions. Conversely, in those with compromised immune systems, adenovirus infections may become severe, potentially advancing to multi-organ failure and resulting into 55% mortality.[1]

Acute respiratory infections are the leading cause of morbidity and mortality globally, but medications and antivirals are only effective against one or two viruses.[2]

Human adenovirus (HAdV) is one of the most significant viruses encountered in clinical settings and public health today. This is associated with a wide range of illnesses ranging from benign colds to more serious conditions including gastroenteritis, acute respiratory infections, conjunctivitis, haemorrhagic cystitis, meningoencephalitis and can cause severe disease in younger children.[3] Hospitalization and mortality have been linked to respiratory HAdV's alone or in co-infection with other respiratory viruses in most of the paediatric population.[4]

Despite accounting for a considerable percentage of respiratory infections, there are relatively few reports of

respiratory HAdV's from India.[5,6] Current study focuses on prevalence of adenoviral associated disease, risk factors, clinical manifestations and treatment in paediatric patients.

METHODS

Study design

It was a prospective, observational, single centre study.

Study sample

The study included 100 children diagnosed with adenovirus.

Inclusion criteria

The study includes patients, patient care takers who are willing to participate, both male or female children diagnosed with adenovirus associated diseases aged between 1 month to ≤15 years of age.

Exclusion criteria

The study excludes patients, patient care takers who are not willing to participate, neonates and children above 15 years of age.

Study site

The current study is a single-centre, hospital-based investigation conducted between July 2023 to December 2023 in the department of Paediatrics, Yashoda Hospital, Secunderabad, which is accredited by the NABH and NABL.

Selected patients were advised for blood test, C-reactive protein (CRP) test and respiratory panel test. Medical history, physical examination and test results were analysed and patients detected with adenovirus positive has been selected to find the prevalence of adenovirus associated disease, clinical manifestation and treatment.

Statistical analysis

Statistical analysis was performed using IBM statistical package for the social sciences (SPSS) V26.0. Mean±SD was used to present the quantitative data, Mann-Whitney test was used if the data failed the "normality test," and the unpaired t-test was used if the data passed. Number (%) was used to present the results of categorical measurements.

Fisher's exact test and the Chi-square test with continuity correction were used to evaluate the associations between the qualitative variables in all two-by-two tables. $P<0.05$ was considered statistically significant.

RESULTS

Table 1 shows that, majority of patients (51%) were between the ages of 1 and 5 years, followed by 6 to 10 years (24%), 1 month to 1 year (21%) and 11 to 15 years (4%). Out of 100 patients, 55% were males and 45% were females. The clinical manifestations show that, all patients had fever (100%) with cough (79%), cold (67%), vomiting (34%), SOB (18%), loose stools (13%), noisy breathing (12%), abdominal pain (12%), sore throat (10%), headache (5%), conjunctivitis (3%) and ear pain (1%).

Table 1: Age, gender and clinical manifestation of patients with adenovirus positive.

Characteristics	Frequency (N)	Percentage
Age (years)		
<1	21	21
1-5	51	51
6-10	24	24
11-15	4	4
Gender		
Male	55	55
Female	45	45
Clinical parameters		
Fever	100	100
Cold	67	67
Cough	79	79
Shortness of breath	18	18
Loose stools	13	13
Vomiting's	34	34
Abdominal pain	12	12
Ear pain	1	1
Sore throat	10	10
Noisy breathing	12	12
Conjunctivitis	3	3
Headache	5	5

The clinical symptoms seen in different age groups are presented in Table 2. Among patients under the age of one year, 100% experienced fever, 66.7% reported cold symptoms, 95.2% suffered from cough, 28.6% exhibited shortness of breath, 28.6% had loose stools and 38.1% experienced vomiting. In the age group of 1 to 5 years, fever was also present in 100% of patients, with 70.6% affected by cold symptoms, 84.3% suffering from cough, 21.6% experiencing shortness of breath, 5.9% reporting loose stools, and 27.5% affected by vomiting. For those aged 6 to 10 years, 100% reported fever, while 58.3% had cold symptoms, 50% suffered from cough, 4.2% exhibited shortness of breath, 8.3% experienced loose stools, and 50% reported vomiting. In the 11 to 15-year age group, 100% of patients experienced fever, 75% had cold symptoms, and 100% suffered from cough, with no patients exhibiting shortness of breath or vomiting; however, 50% reported loose stools. Notably, no statistical differences were identified among the age groups except for cough and loose stools ($p=0.001$, $p=0.007$).

Table 3 lists the comorbidities of children tested positive for the human adenovirus. 75% patients were without comorbidities whereas 25% had. Among the patients with comorbidities, 18% have HADV+ gastroenteritis + dehydration, HADV+ adenoid hypertrophy, HADV+ tonsillar hypertrophy and HADV+ sepsis, while 7% have HADV+ sickle thalassemia, HADV+ pansinusitis, HADV+ shock with down syndrome.

Table 4 elucidates the comorbidities observed in various age groups. HADV + sickle thalassemia, HADV + pansinusitis observed only in 6-19 years age group patients and HADV + shock with down syndrome in 1-5 years age group. HADV + gastroenteritis with dehydration was reported in age groups 1-5 years (66.7%) and 6-10 years (33.3%). HADV + adenoid hypertrophy was maximum (60%) in 1-5 years age group whereas HADV + tonisillar hypertrophy was maximum (75%) in 6-10 years age group with nil report in <1 year and 11-15 years age group. Maximum HADV + sepsis (50%) was identified in 1-5 years age group but 0% in 6-10 years age group.

Table 2: Age wise distribution of patients with clinical symptoms.

Clinical parameters	Age (years) (%)								P value
	<1		1-5		6-10		11-15		
	Yes	No	Yes	No	Yes	No	Yes	No	
Fever	100	0	100	0	100	0	100	0	0.5
Cold	66.7	33.3	70.6	29.4	58.3	41.7	75	25	0.7
Cough	95.2	4.8	84.3	15.7	50	50	100	0	0.001
SoB	28.6	71.4	21.6	78.4	4.2	95.8	0	100	0.1
Loose stools	28.6	71.4	5.9	94.1	8.3	91.7	50	50	0.007
Vomitings	38.1	61.9	27.5	72.5	50	50	0	100	0.1
Abdominal pain	0	100	23.5	76.5	0	100	0	100	0.004
Ear pain	0	100	2	98	0	100	0	100	0.8
Noisy breathing	19	81.0	9.8	90.2	12.5	87.5	0	100	0.0
Conjuctivities	0	100	5.9	94.1	0	100	0	100	0.6
Headache	0	100	3.9	96.1	12.5	87.5	0	100	0.3
Sore throat	0	100	5.8	94.2	20.8	79.2	50	50	0.2

Table 3: Distribution of patients with comorbidities.

Comorbidities	Frequency (N)	Percentage
Distribution of patient		
Patient without comorbidities	75	75
Patient with comorbidities	25	25
Comorbidities		
HADV + gastroenteritis with dehydration	5	5
HADV + adenoid hypertrophy	5	5
HADV + tonsillar hypertrophy	4	4
HADV + sepsis	4	4
HADV + sickle thalassemia	2	2
HADV + pansinusitis	3	3
HADV + shock with Down syndrome	2	2

Table 4: Age wise distribution of patients with comorbidities.

Comorbidities	Age (years) (%)			
	<1	1-5	6-10	11-15
HADV + gastroenteritis with dehydration	0	66.7	33.3	0
HADV + adenoid hypertrophy	20	60	20	0
HADV + tonsillar hypertrophy	0	25	75	0
HADV + sepsis	25	50	0	25
HADV + sickle thalassemia	0	0	100	0
HADV + pansinusitis	0	0	100	0
HADV + shock with Down syndrome	0	100	0	0
P value	0.7	0.5	0.6	0.5

Table 5 explains that majority of patients were hospitalized for 1-5 days (44%) and 6-10 days (44%) whereas lowest (1%) for 16-20 days. Results depict that, 52% of patients had not received Azithromycin. Majority of patients who received Azithromycin were on second day of admission (14%) followed by third (13%) and fourth day of admission (9%). Results also show that, 69% of patients required nebulization support, 2% of patients were with HNFC support, 2% with O_2 support and 1% with HFNC/O_2 support.

Table 5: Duration of hospitalization and Azithromycin started day.

Variables	Frequency (N)	Percentage
Duration of hospitalization (days)		
1-5	44	44
6-10	44	44
11-15	11	11
16-20	1	1
Azithromycin started on day of admission		
Not given	52	52
First day	12	12
Second day	14	14
Third day	13	13
Fourth day	9	9
Type of respiratory support		
HNFC	2	2
O_2	2	2
HFNC/O_2	1	1
Nebulization	69	69

DISCUSSION

HAdVs are commonly implicated in respiratory infections among paediatric populations, affecting both immunocompetent and immunocompromised children.[7] These infections pose significant clinical challenges concerning differential diagnosis and the formulation of effective treatment strategies. To date, the number of clinical studies explicitly investigating HAdV infections within the paediatric demographic remains limited highlighting an urgent need for further research in this domain.[8]

In our research, 51% of the participants were under the age of 5 years, this finding aligns with the observations made by Zhong and Dong, who also reported that 51% of the children were below this age threshold.[9] Furthermore, a significantly higher prevalence was noted in a study involving 87 hospitalized children in Korea, conducted nearly two decades ago (1990-1998), where 71% of the children were under 2 years old and 94% were under 5 years old.[10]

In our study, male children were more significantly affected than female. High number of HAdV infections in males compared to females could be attributed to social and cultural reasons where the probability of bringing a male child to a healthcare facility for treatment is higher compared to a girl child.[11,12] The main symptoms identified in paediatric patients with confirmed adenovirus infections include fever and complications affecting multiple systems, such as cough, respiratory distress, diarrhea, encephalopathy, seizures, shock and cardiac problems.[13,14]

In our research, children with adenovirus infections were also noted symptoms like fever, multisystem involvement, cough, cold, pain, diarrhea, vomiting, headaches and conjunctivitis. Previous research has indicated that a fever lasting 7 days or more is an independent risk factor for severe adenoviral pneumonia. However, in our study the average duration of fever was recorded at 3 days.

Gupta et al documented severe complications, including acute respiratory distress syndrome (ARDS) in 100% of cases, renal failure in 33%, and liver failure in 33% among children with pre-existing health conditions.[15] Additionally, Shieh et al reported instances of myocarditis and cardiomyopathy, while our observations included gastroenteritis, adenoid hypertrophy, tonsillar hypertrophy, sepsis, and sickle thalassemia. In general, the clinical characteristics of respiratory infection may vary age of the patients and the immune system.[16]

Our study provides the brief details of the symptoms, comorbidities, age, duration of fever, duration of hospital stay, nebulization, O_2 support/HNFC support and guidelines provided to the parents regarding adenovirus infection and preventive measures. Normal respiratory support tools for paediatric adenovirus pneumonia include non-invasive mechanical ventilation, a high-flow nasal cannula (HFNC), high-frequency oscillatory ventilation, and invasive mechanical ventilation.[17]

CONCLUSION

The clinical characteristics of respiratory infections with adenovirus vary upon the age of the patients and the immune status. The majority of adenovirus infections are mild and can be effectively managed through rest and the use of over-the-counter pain relievers or fever reducers to alleviate symptoms. There is a requirement for an extensive study of adenovirus in respiratory infections in children with different ages and immune status.

ACKNOWLEDGEMENTS

Authors would like to thank Management Yashoda Hospitals and Dr. Amidyala Lingaiah (Director-Medical Services) for the continuous support.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Darisetty S, Darisetty R, Ahmed I, Arundati P, Thanveer P, Sumana. Prevalence of adeno virus associated diseases among pediatric population in a tertiary care teaching hospital. Int J Contemp Pediatr 2025;12:1120-4.