

Clinical Spectrum of Adenovirus Infection in Hospitalised Children: A Retrospective Study from Hyderabad, Telangana, India

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ABSTRACT

Introduction: Human adenoviral infections, though prevalent among children, are often under-reported. Although adenoviral infections are usually self-limiting, they can cause significant morbidity and hospitalisations in children.

Aim: To evaluate the demographic, clinical, laboratory and radiological characteristics of paediatric patients hospitalised with Human Adenovirus (HAdV) infection.

Materials and Methods: This was a hospital-based retrospective study conducted in the Paediatric Outpatient Department (OPD) and inpatient wards of Rainbow Children's Hospital, Hyderabad, Telangana, India for a period of 11 months from February 2023 to December 2023. A total of 210 children aged one month to 16 years who tested positive for adenovirus by Polymerase Chain Reaction (PCR) on a nasopharyngeal swab were included in the study. The demographic, clinical, laboratory, and radiological profiles of these cases were analysed. The statistical analysis was performed using the IBM Statistical Package for Social Sciences (SPSS) software version 27.0 (Armonk, NY, USA).

Results: Of the 210 children who tested positive for adenovirus, 126 (60%) were males and 129 (61.42%) were between one and five years of age. Notably, 141 children (67.14%) were hospitalised during the summer season. Most cases occurred during the summer months, predominantly among males aged

1-5 years. Symptoms included high-grade persistent fever in 205 cases (97.62%), cough and cold in 129 (61.42%), vomiting in 59 (28.1%) and loose stools in 27 (12.86%). Less frequent presentations were pneumonia in 12 cases (5.71%), seizures in 8 (3.81%), burning micturition in 5 (2.38%) and conjunctivitis in 4 (1.9%). Children were categorised into three groups: A, B and C- based on their clinical presentation as respiratory, gastrointestinal or mixed types, respectively. A significant difference in C-Reactive Protein (CRP) distribution was observed among the three groups (p-value <0.0001). CRP positivity (>10 mg/L) was most frequent in group A, 78/99 (78.8%), followed by group C 36/52 (69.2%), while group B showed a lower proportion 21/59 (35.6%). Group A children had significantly higher CRP levels and a longer duration of fever. Of the 210 cases, 195 children (92.86%) were treated with antibiotics.

Conclusion: The HAdV infections present with high-grade fever and respiratory symptoms are their predominant manifestation. HAdV infections should be considered as a differential diagnosis in children with prolonged fever and multisystem involvement. In addition, gastrointestinal involvement was common. All children had favourable outcomes and were discharged without any complications. Early and accurate diagnosis of HAdV infection using rapid diagnostic tests prevents unnecessary antibiotic use and aids parental counselling and should be routinely employed.

Keywords: C-reactive protein, Gastroenteritis, Polymerase chain reaction, Viral pneumonia

INTRODUCTION

The HAdVs were first isolated in 1953 by Rowe WP et al., from human adenoid tissue explants [1]. HAdVs are non enveloped, double-stranded Deoxyribonucleic Acid (DNA) viruses of the family Adenoviridae, comprising more than 50 genotypes grouped into seven species (A-G). [2] They are transmitted mainly via respiratory droplets, the faecal-oral route and contaminated surfaces and are notable for their stability in the environment [1,2]. HAdVs cause a wide spectrum of illnesses in children, including the common cold, respiratory tract infections, conjunctivitis, and gastroenteritis, while occasionally leading to systemic illnesses such as haemorrhagic cystitis, hepatitis, myocarditis and encephalitis, especially in immunocompromised hosts [3,4]. Although infections are usually self-limiting, they can cause significant morbidity and hospitalisations in paediatric populations.

The incidence of HAdV infection in children with respiratory tract infections is estimated to be 7-10%, although the exact rate remains uncertain due to the limited use of diagnostic testing [2-5]. Certain HAdV serotypes are mainly linked to respiratory tract infections (types 1-5, 7,14,21), while others, such as types 40 and 41, are associated with gastroenteritis [1,5-7]. Children with respiratory or systemic HAdV infections can shed the virus for 3-6 weeks,

leading to easy transmission among children and individuals in closed settings such as daycare centres, orphanages and similar institutions [3,6-8].

HAdVs predominantly affect children under five years of age. Symptomatic HAdV infections typically present with high-grade, prolonged fever and elevated inflammatory cytokines [9,10]. Consequently, CRP levels are often markedly raised, which may lead to unwarranted antibiotic use and hospital admissions [9]. In early 2023, a sharp rise in paediatric hospital admissions was noted for acute febrile illnesses with multisystem involvement. Children frequently presented with respiratory symptoms (cough, cold, breathlessness), gastrointestinal disturbances (loose stools) and, in some cases, neurological manifestations such as seizures. Given the limited published data on adenovirus infections from India [11-13], the current study was undertaken to address this gap by evaluating the demographic, clinical, laboratory and radiological characteristics of children hospitalised with HAdV infection.

MATERIALS AND METHODS

This was a hospital-based retrospective study conducted in the Paediatric OPD and inpatient wards of Rainbow Children's Hospital, Hyderabad, Telangana, India. Medical records of children aged one month to 16 years diagnosed with HAdV infection and admitted

over 11 months from February 2023 to December 2023 were reviewed. Data were retrieved from the hospital's electronic medical database and individual case sheets. Data extraction, analysis and interpretation were performed between December 2024 and January 2025. The study was approved by the Hospital Ethics Committee (Reference No: RCH-EC/NOV/24-PAED-11).

Inclusion criteria: Children aged one month to 16 years, presenting with fever, cough, loose stools and multisystem involvement (≥ 2 systems) were screened for adenovirus infection. Children aged one month to 16 years, admitted with a positive PCR (nasopharyngeal swab) for adenovirus, were included in the study.

Exclusion criteria: Children with a positive blood culture for bacterial pathogens and those who tested positive for other respiratory viruses, including parainfluenza virus, rhinovirus, Respiratory Syncytial Virus (RSV), influenza virus and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), were excluded from the study.

Sample size: During the 11-month study period from February 2023 to December 2023, a total of 210 children aged one month to 16 years who tested positive for HAdV infection and fulfilled the inclusion criteria were included in the study. As this was a retrospective study including all consecutive eligible cases during the study period, no prior sample size calculation was performed. Supportive and symptomatic management was provided to all patients.

Study Procedure

The identity of patients with HAdV infection was kept confidential. The objective was to describe the demographic, clinical, laboratory, and radiological profile of these cases. Confirmation of HAdV infections occurred during the hospital stay, using the nasopharyngeal swab RT-PCR test. Trained technicians collected nasopharyngeal swabs and transported them in Viral Transport Medium (VTM) under cold chain conditions to the Department of Clinical Microbiology, Central Laboratory, Rainbow Children's Hospital, Banjara Hills, Hyderabad. The vials on receipt were vortexed and centrifuged at 1500 rpm for 5 minutes before nucleic acid extraction.

Nucleic acid extraction was carried out on all the samples using the QIAamp DNA Mini Kit (QIAGEN GmbH, Hilden, Germany) as per the manufacturer's instructions. Around 110 μ L of viral nucleic acid was extracted in the final step from a total sample volume of 400 μ L. RT-PCR was performed on a QuantStudio™ 5 RT-PCR System (Applied Biosystems, Thermo Fisher Scientific, Waltham, MA, USA) using the Altona HAdV PCR assay. Cycle threshold (Ct) and viral load correlation were done by extrapolating the adenoviral load from the Ct value using the provided standards as a reference. The result was considered positive if the melting curve crossed the threshold line within 40 cycles ($Ct < 40$).

Children were categorised into three groups- A, B and C- based on their clinical presentation as respiratory, gastrointestinal, or mixed types, respectively [14]. Based on the clinical presentation of HAdV infections, patients were categorised into the following groups:

Group A: Patients presenting with only respiratory tract symptoms, including Acute Otitis Media (AOM), upper respiratory tract infections (such as rhinitis, pharyngotonsillitis and laryngitis) and Lower Respiratory Tract Infections (LRTI), such as bronchiolitis and pneumonia. The diagnosis of LRTI was established clinically and/or confirmed by chest X-ray.

Group B: Patients presenting with only gastrointestinal symptoms, including diarrhoea and vomiting.

Group C: Patients presenting with both respiratory and gastrointestinal symptoms.

The clinical profile, laboratory parameters and hospital stay were analysed. Age group, CRP values, duration of fever and hospital stay were compared among the three groups.

STATISTICAL ANALYSIS

Descriptive statistics were used for the representation of frequency, mean and Standard Deviation (SD). Data not following normal distribution were represented as median and Interquartile Range (IQR). Categorical variables were compared using the Chi-square or Fisher's-exact test, as appropriate. Continuous data were compared using the Kruskal-Wallis test. A p-value of <0.05 was considered statistically significant. The statistical analysis was performed using the IBM SPSS version 27.0 software (Armonk, NY, USA).

RESULTS

A total of 210 children were diagnosed with HAdV infection. Respiratory symptoms alone were seen in 99 (47.14%), gastrointestinal symptoms alone in 59 (28.09%) and both systems were involved in 52 (24.76%) children. None developed severe disease requiring mechanical ventilation or dialysis. The highest proportion of cases occurred in the 1-5 years age group, 129 cases (61.42%), followed by >five years, 61 cases (29.04%) and <one year 20 (9.52%), with a significant age-related difference (p -value <0.0001) [Table/Fig-1]. However, age distribution across clinical groups was comparable (p -value=0.609) [Table/Fig-2]. A significant seasonal variation was observed, with most cases observed during summer, 141 (67.14%), followed by winter 45 (21.43%), monsoon 16 (7.62%) and post-monsoon 8 (3.81%) (p -value <0.0001). A male predominance was also noted (126 vs. 84; p -value=0.0038) [Table/Fig-1].

Parameters	n (%)
Age (in years)	
< 1	20 (9.52)
1 - 5	129 (61.42)
> 5	61 (29.04)
Gender	
Male	126 (60)
Female	84 (40)
Seasonal distribution	
Winter	45 (21.43)
Summer	141 (67.14)
Monsoon	16 (7.62)
Post-monsoon	8 (3.81)

[Table/Fig-1]: Demographic characteristics of patients., N=210.

Age, gender and seasonal distributions of adenovirus cases showed significant variation. Most cases were aged 1-5 years ($p < 0.001$), were male ($p = 0.0038$) and occurred in summer ($p < 0.001$).

Variables	Group A (n= 99)	Group B (n= 59)	Group C (n= 52)	p-value
Age (in years)				
< 1	11	4	5	0.609
1-5	60	34	35	
>5	28	21	12	
Gender				
Males	58	37	31	0.875
Females	41	22	21	

[Table/Fig-2]: Age and gender-wise distribution of HAdV cases according to groups.

The age and gender distributions were comparable among the three groups with no statistically significant difference (age: $p = 0.609$; gender: $p = 0.875$).

Of the 210 children evaluated, 205 (97.62%) had fever at the time of presentation. Respiratory symptoms were the most common manifestation, with cough and cold in 129 (61.42%) and pneumonia in 12 cases (5.71%). Gastrointestinal symptoms included vomiting in 59 (28.09%) and loose stools in 27 (12.85%) cases. Neurological involvement in the form of seizures was seen in 8 (3.8%) children. Urinary symptoms (burning micturition) occurred in 5 (2.38%),

conjunctivitis in 4 (1.9%), tonsillar enlargement in 6 (2.85%) and lymphadenopathy in 4 (1.9%) cases. Fever as the sole symptom was noted in 12 (5.71%) children [Table/Fig-3].

Clinical parameters	n (%)
Fever	205 (97.61)
Common cold	129 (61.42)
Cough	113 (53.81)
Vomiting	59 (28.1)
Loose stools	27 (12.86)
Pneumonia	12 (5.71)
Seizures	8 (3.81)
Enlarged tonsils	6 (2.85)
Dysuria	5 (2.38)
Lymphadenopathy	4 (1.9)
Conjunctivitis	4 (1.9)
Rash	3 (1.42)

[Table/Fig-3]: Clinical characteristics of patients with HAdV.

Anaemia (Hb<10 g/dL) was observed in 38 (18.09%) children. Leukocytosis (>10,000/cu.mm) was present in 106 (50.47%), with neutrophilic predominance in 148 (70.4%). Elevated CRP levels (>50 mg/L) were noted in 80 (38.09%) cases, including 32 (15.2%) with CRP >100 mg/L. CRP positivity (>10 mg/L) differed significantly among the three groups (p-value <0.001), being highest in group A (78.7%), followed by group C (69.2%) and lowest in group B (35.5%) (p-value <0.001). Blood cultures were negative in all cases [Table/Fig-4,5].

Laboratory parameters	n (%)
Haemoglobin (g/dL)	
< 10	38 18.09
>10	172 81.9
WBC (per cu.mm)	
<4000	17 8.09
4000 - 10000	87 41.42
>10000	106 50.47
Differential count (%)	
Neutrophilia	148 70.47
Lymphocytosis	62 29.52
Platelets (Lacs/cu.mm)	
<1.5	7 3.33
>1.5	203 96.67
CRP (mg/L)	
<10	75 35.71
10-50	55 26.19
51-100	48 22.86
>100	32 15.24
SGOT (U/L)	
<40	171 81.42
>40	39 18.57
SGPT (U/L)	
<40	201 95.71
>40	9 4.28

[Table/Fig-4]: Laboratory characteristics of patients with HAdV. WBC: White blood cell count; CRP: C-reactive protein; SGOT: Serum glutamic-oxaloacetic transaminase; SGPT: Serum glutamic-pyruvic transaminase

Chest X-ray was performed in 83 children, showing bilateral paracardiac infiltrates in 64 (30.47%), patchy opacities/consolidation in 12 (5.71%) and pleural effusion in one case [Table/Fig-6]. Abdominal ultrasonography in 76 children revealed mesenteric

C-Reactive Protein (mg/L)	Group A (n= 99)	Group B (n= 59)	Group C (n= 52)	p-value
<10	21	38	16	< 0.001
10-50	27	11	17	
50-100	30	7	11	
>100	21	3	8	

[Table/Fig-5]: CRP values of HAdV cases according to groups. There is a highly significant difference (p<0.001) in CRP distribution among the three groups; Group A has more patients with higher CRP, while Group B had low CRP, showing clear variation.

X-ray findings	n (%)
Bilateral paracardiac infiltrates	64 (30.47)
Patchy opacities	9 (4.28)
Left lower lobe haziness	6 (2.85)
Lobar consolidation	3 (1.42)
Pleural effusion	1 (0.47)

[Table/Fig-6]: Chest radiography findings.

lymphadenitis in 32 (15.23%) and free fluid or organomegaly in 22 (10.47%). Antibiotics were administered in 195 (92.85%) children, with 51.9% receiving two agents; de-escalation was done in 21 (10%) cases. Median fever duration differed significantly among groups {5 (3-6), 2 (1-2) and 3 (1-4) days; p-value <0.001}, while hospital stay was comparable {5 (3-6), 4 (3-5) and 4 (3-5) days; p-value=0.21} [Table/Fig-7].

Variables	Group A	Group B	Group C	p-value ¹
Duration of fever (days), Median (IQR)	5 (3-6)	2 (1-2)	3 (1-4)	<0.001
Hospital stay (days), Median (IQR)	5 (3-6)	4 (3-5)	4 (3-5)	0.21

[Table/Fig-7]: Comparison of duration of fever and hospital stay among the three groups. ¹Kruskal-Wallis test; There was a statistically significant difference in the duration of fever among the groups (p<0.001), whereas the length of hospital stay did not differ significantly (p=0.21).

DISCUSSION

The present retrospective study analysed the demographic characteristics, clinical presentation, laboratory, and radiological parameters of adenoviral infection in children aged one month to 16 years. Children with HAdV infections were categorised into three groups- A, B and C-based on their clinical presentation as respiratory, gastrointestinal or mixed types, respectively.

In the present study, the majority of children affected were below five years of age (70.95%), a finding consistent with previous reports by Dutta S et al. and Shachor-Meyouhas Y et al., [11,15]. The higher susceptibility in younger children may be attributed to greater environmental exposure and immature immunity. Although male children were affected more frequently than females, no statistically significant difference in gender distribution was observed between the three groups. Similar male predominance has been reported in studies from India, Malaysia and Taiwan, suggesting a possible gender-related susceptibility that warrants further investigation [11-13,16,17].

Admissions peaked during the summer months, accounting for 67.14% of cases, indicating a clear seasonal trend similar to that reported by Dutta S et al., [11]. Adenovirus infections, which commonly involve the respiratory and gastrointestinal systems, may demonstrate seasonal variation due to environmental factors and increased social interactions. More than half of the children presented with cough (53.8%), which is also comparable to observations reported by Dutta S et al., [11]. In the present study, fever was the most consistent presenting symptom observed in all children, in agreement with findings reported by Ptak K et al. and Rajbanshi A et al., [14,18].

Leukocytosis was observed in 50.4% of children in the present study, which is higher than that reported by Dutta S et al., (20%)

S. No.	Author's name and year	Type and place of study	Sample size	Objectives	Diagnosis	Conclusion
1	Shachor-Meyouhas Y et al., 2019 [15]	Retrospective 9 years study, Israel	956	HAdV infection in PICU cases	Real-time PCR, immunofluorescence	8.2% mortality in PICU admitted cases
2	Shi J et al., 2020 [19]	Single centre retrospective observational study, China	67	Risk factors and outcome	Real-time PCR on nasopharyngeal swab, BAL	Liver dysfunction and sepsis associated with poor outcome. 16.4% mortality
3	Rajbanshi A et al., 2022 [18]	Single-center, prospective study, India	96	Epidemiological, clinical, biochemical and radiological profile of severe pneumonia	Real-time PCR on nasopharyngeal swab	34% had severe pneumonia. 27.3% mortality
4	Ptak K et al., 2023 [14]	Single centre retrospective observational study, Poland	135	To correlate clinical picture with serology	Real-time PCR on nasopharyngeal swab and stool	Fever and high CRP present in respiratory group
5	Majumdar A et al., 2023 [13]	Multi center observational study, India	1154	Clinical, laboratory, demography, radiological profile	Nucleic acid extraction, genotyping, Phylogenetic analysis	1.6% mortality
6	Dutta S et al., 2024 [11]	Single centre retrospective study, India	25	Clinical, laboratory, demography, radiological profile	Real-time PCR on nasopharyngeal swab (Respiratory panel 5)	High prevalence in summer. No mortality. Fever predominant symptom (100% cases)
7	Varadarajan P et al., 2024 [12]	Single centre observational study, India	130	Clinical profile & risk factors for mortality	Real-time PCR on nasopharyngeal swab, Endotracheal aspirate	41.3% required intensive care. Multi-system involvement. 13% mortality
8	Present study	Single centre retrospective study, India	210	Clinical, laboratory, demography, radiological profile	Real time PCR, Nucleic acid extraction	Fever predominant symptom. High CRP. No mortality

[Table/Fig-8]: Comparison of studies on adenovirus.

BAL: Broncho alveolar lavage; CRP: C-reactive protein; PCR: Polymerase chain reaction; PICU: Paediatric intensive care unit

and Chen HL et al., (23.8%) [11,17]. Neutrophilic predominance was seen in 70.4% of children, though no statistically significant difference was observed among the three groups. Adenoviruses are pro-inflammatory and these findings reiterate the well-known overlap between the inflammatory profile of adenoviral and bacterial infections [9,14].

The CRP levels showed a significant difference among the three groups. CRP positivity (>10 mg/L) was considerably higher in group-A, indicating an inflammatory response. Ptak K et al., also classified HAdV infections into three clinical groups and observed that children presenting with respiratory manifestations had higher CRP levels [14]. In the present study, children with predominant gastrointestinal symptoms did not show significant CRP elevation, which may be explained by the tissue tropism of different adenoviral serotypes. A markedly elevated CRP (>50 mg/L) was observed in 38.09% of children, which is lower than that reported by Dutta S et al., (80%) and Rajbanshi A et al., (67%) [11,18]. Elevated SGPT levels were seen in only 4.28% of cases, a finding consistent with studies by Dutta S et al. and Chen HL et al., both of which reported transaminase elevation in approximately 4% of children [11,17].

Radiologically, a greater proportion of children demonstrated bilateral paracardiac infiltrates than lobar consolidation, similar to the findings of Dutta S et al., [11]. In contrast, studies from China reported a higher prevalence of consolidation and severe pneumonia with certain virulent adenoviral serotypes [19].

These findings suggest that HAdV infections frequently present with high-grade and prolonged fever, challenging the traditional perception that they are primarily respiratory illnesses. Gastrointestinal manifestations were also reported with significant frequency.

Despite the viral aetiology, the majority of children (92.8%) in the present study received antibiotics and more than half received two antibiotics. De-escalation of antibiotic therapy occurred in only 10% of cases. Although rapid diagnostic tests allow prompt and accurate identification of HAdV infections, they are still not routinely used in many clinical settings [20-24]. Early identification of adenoviral infection using PCR is critical, as it enables appropriate clinical management and helps avoid unnecessary antibiotic use often prompted by its bacterial-like presentation with elevated CRP, leukocytosis and neutrophilia [10,14].

None of the patients developed severe complications such as hepatitis, myocarditis, or required mechanical ventilation or intensive care support. There was a statistically significant difference in the duration of fever among the groups, with children in group A having a longer febrile course. However, the length of hospital stay did not differ significantly between the groups. No mortality occurred among children with HAdV infection in the present cohort, indicating a generally favourable clinical course, consistent with the findings of Dutta S et al., [11]. This could be due to infection with less virulent serotypes; however, serotyping was not undertaken in the present study. Unlike the present study, Varadarajan P et al., Rajbanshi A et al. and Shi J et al., reported higher mortality, likely reflecting a cohort of more severely ill children with multi-system involvement requiring intensive care [12,18,19]. Similar studies have been tabulated in [Table/Fig-8] [11-15,18,19].

This large single-centre study provides valuable insight into the demographic profile, clinical spectrum, laboratory and radiological features of adenoviral infection in hospitalised children. The findings reinforce the importance of considering HAdV as a major cause of febrile illness in young children and highlight the critical role of early and accurate diagnosis in optimising patient management and minimising unnecessary antibiotic use.

Limitation(s)

A key limitation of this study is the absence of serotype analysis of the identified HAdV strains, which precluded assessment of potential associations between specific serotypes and their corresponding clinical manifestations. Stool samples were not tested, which might have led to underdiagnosis of certain HAdV infection cases.

CONCLUSION(S)

The present study demonstrates that HAdV is a significant cause of febrile illness and hospitalisation in children, particularly in those under five years of age. The infection commonly presents with high-grade and prolonged fever, respiratory symptoms and a bacterial-like inflammatory response with elevated CRP and leukocytosis, often leading to unnecessary antibiotic use. Despite marked inflammatory markers, the overall clinical course was mild in most children, with no mortality and no requirement for intensive care or mechanical

ventilation. Distinct differences in inflammatory response and duration of fever were observed among the clinical groups, although the length of hospital stay remained similar. Early and accurate molecular diagnosis of adenovirus reduces inappropriate antibiotic use, guides targeted management and improves antimicrobial stewardship in paediatric practice.

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