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Original Research Article

CLINICAL, LABORATORY CHARACTERISTICS AND OUTCOMES OF SEVERE PNEUMONIA IN CHILDREN UNDER 5 YEARS OLD WITH AND WITHOUT ADENOVIRUS INFECTION

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Abstract

Background: Adenovirus is frequently seen in children with severe pneumonia and severe pneumonia can result in long-term problems. To identify the differences of clinical characteristics and outcomes of severe pneumonia in children under 5 years old with and without adenovirus infection. **Materials and Methods:** It was retrospective study conducted for a period of 5 years from April 1, 2018, to March 31, 2023 in tertiary care hospital were recorded. Depending on whether or not they satisfied the following inclusion criteria, all paediatric patients were included: 5 years old; clinical symptoms suggestive of pneumonia, acquired outside the hospital or 48 hours after hospital admission; met severe pneumonia criteria as defined by WHO, with at least one of the danger signs: persistent vomiting, convulsions, lethargy, inability to drink/feed, respiratory distress with oxygen saturation less than 90%, or severe malnutrition; took the test for adenovirus infection during the early stage of admission; and were discharged from hospital or died there. **Result:** Out of 525 severe pneumonia children enrolled in this study, 43 (8.2%) had an adenovirus infection. The fatality rate of cases with adenovirus infection (9.3%) was higher than cases without adenovirus infection (2.5%). More than two-thirds of the severe pneumonia paediatric cases were <1 year old, but most cases with adenovirus infection were older than 1 year old. all children with severe pneumonia had greater Neutrophil counts, haemoglobin levels, and lower albumin levels, according to standard blood tests and blood biochemistry; however, these three factors were lower in cases with viral infection than in patients without adenovirus infection. **Conclusion:** Children with severe pneumonia who also had an adenovirus infection had more aberrant laboratory results and more serious clinical outcomes. The consequences of viral infection require more consideration.

INTRODUCTION

15% of all child fatalities globally are attributable to pneumonia, which is also a major reason for hospitalization.[1] Adenovirus is frequently seen in children with severe pneumonia and severe pneumonia can result in long-term problems. Adenoviruses are widespread throughout the world and shouldn't be disregarded because they can lead to serious and even fatal pneumonia.[2] Adenovirus detections from hospitalized patients with severe respiratory infections increased in the USA in 2014.[3] Adenoviruses have been found to be the primary pathogens linked to severe paediatric pneumonia.[4] Additionally, severe adenovirus-associated pneumonia is gaining more and more attention globally.[5]

Because some adenovirus serotypes are linked to particular clinical symptoms, they have been the subject of numerous prior research.[6] Clinicians, with the exception of researchers, cannot further discover the serotypes of specific infections using PCR because of the high cost and slow turnaround time for test findings.[7] The lack of recognizable clinical signs of adenovirus, one of the most often detected viruses from young infants with febrile respiratory disease, presents difficulties for doctors. Furthermore, information on the epidemiology, clinical characteristics, test results, and outcomes of severe pneumonia among adenovirus infections is still scarce.

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MATERIALS AND METHODS

It was retrospective study conducted for a period of 5 years from April 1, 2018, to March 31, 2023 in tertiary care hospital were recorded. Depending on whether or not they satisfied the following inclusion criteria, all paediatric patients were included: 5 years old; clinical symptoms suggestive of pneumonia, acquired outside the hospital or 48 hours after hospital admission; met severe pneumonia criteria as defined by WHO, with at least one of the danger signs: persistent vomiting, convulsions, lethargy, inability to drink/feed, respiratory distress with oxygen saturation less than 90% or severe malnutrition; took the test for adenovirus infection during the early stage of admission; and were discharged from hospital or died there. And the following cases were excluded: those with significant data gaps and those without an adenovirus result. Based on the results of an X-ray, a doctor can determine whether a child has pneumonia, bronchitis, bronchiolitis, or any combination of the three [8]. A total of 525 severe pneumonia patients with and without adenovirus viral infection were included in this study.

Methodology: We extracted data from electronic medical records on demographics, complications, initial routine laboratory results, therapy records, and clinical outcome. Complete blood counts, virus tests, and biochemistry were all examined in the lab to keep an eye on the myocardial, renal, and hepatic functioning. Hospital length of stay (LOS) in days were clinical outcomes. RT-PCR assays or rapid antigen tests were performed on respiratory tract samples taken from all hospitalized children the same day or the following day to check for common pneumonia pathogens like syncytial virus, adenovirus, and influenza viruses A and B. The samples were taken during ordinary clinical practice and included sputum, throat swabs, nasal swab or bronchoalveolar lavages.

Cases with adenovirus infection were considered if one of the following criteria was met: (1) detection of adenovirus in sputum, throat swabs, nasal swab or bronchoalveolar lavages by RT-PCR; (2) positive antigen in the adenovirus antigen test. Other cases were considered as cases without adenovirus infection. Co-infection was defined as detection of more than one pathogen including viral, bacterial, or atypical pathogens. The study was approved by Institutional Ethics committee. Written informed consent was taken.

Statistical Analysis: The statistical analysis was performed using SPSS for windows version 25.0 software (IBM). The findings were present in number and percentage analyzed by frequency, percent. Chi‑square test was used to find the association among variables. The critical value of P indicating the probability of significant difference was taken as <0.05 for comparison.

RESULTS

As per [Table 1] Of the 525 severe pneumonia children enrolled in this study, 43 (8.2%) had an adenovirus infection. The fatality rate of cases with adenovirus infection (9.3%) was higher than cases without adenovirus infection (2.5%). More than two-thirds of the severe pneumonia paediatric cases were <1 year old, but most cases with adenovirus infection were older than 1 year old. Severe pneumonia children with adenovirus infection were more likely to be boys, older than 1 year old and infected with a combination of other microorganisms, but less likely to have mixed virus infection and co-occurring cardiovascular disease than cases without adenovirus infection.

As per [Table 2] all children with severe pneumonia had greater lymphocyte counts, hemoglobin levels, and lower albumin levels, according to standard blood tests and blood biochemistry; however, these three factors were lower in cases with viral infection than in patients without adenovirus infection. Additionally, compared to individuals without an adenovirus infection, cases with an adenovirus infection exhibited lower lymphocyte levels (5.4–9.92) and greater neutrophil levels. All instances showed longer APTT and greater D-dimer results in the coagulation function test, indicating that all cases with adenovirus infection had worse coagulation function than all cases without viral infection. According to other laboratory results, children with severe pneumonia had higher LDH levels, and adenovirus infections were more common than non-infections. Adenovirus infection victims also had elevated glucose levels. Respiratory distress occurred in 64.0% of adenovirus-infected individuals during hospitalization, compared to 24.7% of adenovirus-uninfected cases. Moreover, adenovirus infection patients stayed lasting longer in the hospital.

Table 1: Demographic and Clinical Characteristics of children with severe pneumonia with and without ADV infection.

Characteristics	Total, n = 525	With ADV infection, n = 43	Without ADV infection, n = 482	P
Gender, n (%)				.04
Male	331(63.04)	30(69.7)	301(62.44)	
Female	194(36.95)	13(30.3)	181(37.55)	
Age at diagnosis (month), median [IQR]	1 (1, 3)	10 (5, 16)	1 (1, 3)	0.01
Age Category, n (%) < 1 year	358	16 (21.3)	342(70.95)	0.01
1–4 years	167	59 (78.7)	108(29.05)	
Co-infection	45	14(2.6)	31(5.9)	0.01

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No pathogen infection	350	-	266	
Viral infection				0.01
Single infection	150(28.5)	56 (74.7)	68(14.1)	
Mixed infection	25(4.76)	19 (25.3)	16(3.3)	
Comorbidities				
Cardiovascular disease	28(5.3)	9 (12.0)	21(4.3)	0.01
Gastrointestinal disease	24(4.5)	9 (16.0)	15(3.1)	0.85
Hepatic and bile disease	8(1.5)	3 (8.0)	5(1.03)	0.94
Renal damage	5(0.95)	1 (1.3)	4(0.82)	0.64
Cerebral damage	21(4)	9 (12.0)	12(2.48)	0.21

Table 2: Laboratory findings and Clinical outcomes of Children

Characteristics	With ADV infection	Without ADV infection	P
Blood routine			
Leucocyte count, ×109/L	9.54 ± 5.56	11.95 ± 7.82	0.01
Lymphocyte count, ×109/L	5.4 ± 9.92	7.45 ± 10.64	0.02
Neutrophil count, ×109/L	3.75 [2.22, 6.47]	4.01	0.01
Lymphocytes, %	32 [23, 46]	46 [32, 56]	0.01
Neutrophils, %	60[44,71]	40[29,55]	0.01
Platelets, %	0.27 [0.18, 0.42]	0.40 [0.31, 0.49]	0.01
Hemoglobin, g/L	10.4+ 2.4	11.2+2.7	0.01
Blood biochemistry			
Albumin, g/L	33.38 ± 6.38	37.26 ± 4.34	0.01
Coagulation function			
APTT, s	43.63 ± 15.89	43.54 ± 7.31	0.01
PT, s	13.68 ± 2.46	13.97 ± 2.68	0.58
D-dimer, mg/L	2.64 [1.38, 4.65]	1.07 [0.54, 2.07]	0.01
Other Laboratory findings			
ALT, U/L	22.0 [15.0,32.5]	20.0 [13.0, 30.3]	0.01
AST, U/L	55.0 [15.0,32.5]	35.0 [28.0, 49.0]	0.01
Total bilirubin, μmol/L	3.8 [2.2,5.9]	24.85 [7.40, 72.0]	0.99
LDH, U/L	646 [464,1378]	328[278, 407]	0.01
BUN, mmol/L	3.91 ± 4.21	3.09 ± 2.69	0.01
Scr, μmol/L	22.88 ± 8.9	25.4 ± 30.37	0.70
CK, U/L	114 [74, 226]	113 [76, 195]	0.01
Glucose, mmol/L	6.25 [5.2, 7.5]	5.5 [4.8, 6.5]	0.01
CRP, mg/L	95 [38, 170]	4.4 [0.6, 10.6]	0.01
PCT	4.4(0.22, 14)	0.55(0.35, 1.2)	
Hospital stay (days)	11(8-19)	7(8-15)	0.01

DISCUSSION

Compared to those without an adenovirus infection, children with severe pneumonia who also had an abnormal laboratory finding had more serious clinical outcomes having higher mortality, longer LOS, and more respiratory failure. In our study, children with severe pneumonia had a median age of 10 months, making them older than children without adenovirus infection. The research in Singapore revealed the median age of children with adenovirus pneumonia in Malaysia was 1.08 years, which was comparable to ours, according to another study, and most paediatric patients with adenovirus infections were under 2 years old.[4,5] Since it has been determined that adenovirus primarily affects those who have impaired immune systems, infants under the age of one may be more susceptible to contracting the virus. More evidence is required to support this theory, however, as fatal cases have also been reported among neonates.[6,7]

There was no statistically significant difference in the prevalence of cardiovascular illness between children with and without adenovirus infections (12% vs. 4.3%) relevance for other illnesses. Prematurity and congenital cardiac conditions are related with disease severity but do not demonstrate statistical significance for adenovirus pneumonia, according to a Taiwanese study.[8] In severe viral infection and pneumonia, respiratory and neurological diseases were more common. Tsou demonstrated that viral infections were more likely to occur in patients with underlying disorders, particularly neurologic illnesses.[9] According to one study on risk factors linked to pneumonia-related deaths in children, malnutrition was the most frequent cause of death.[10] More aberrant laboratory findings were found in cases of severe pneumonia in children with adenovirus infection than in patients without viral infection. Greater severity is indicated by higher LDH levels injuries and suggested a possible hepatitis infection.[11] According to the Erez study, cases of severe pneumonia had high blood levels of LDH, and those with an adenovirus infection had LDH levels that were twice as high as cases without an adenovirus infection. Serum and pleural fluid levels in severe adenovirus respiratory infection were similar according to Lai et al.[12,13] According to Wu et al., a low lymphocyte count and a high blood level of LDH may be utilized as indicators of the severity of an adenovirus respiratory infection in children.[14] Children with severe adenovirus pneumonia and low serum albumin may have a bad prognosis, according to a research by Miao et al,[15] instances of adenovirus CRP levels were greater, which was in line with Chen's study, which showed that raised CRP levels were typical of adenovirus infection, even in the absence of a secondary bacterial infection.[16]

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The present study has few limitations data were frequently insufficient, as they are in most retrospective epidemiological research, and analyses could be skewed. In order to compare an adenovirus infection with a common virus, we were unable to determine different virus infection. Therefore, it is important to use caution when interpreting the results of our study.

CONCLUSION

Children with severe pneumonia who also had an adenovirus infection had more aberrant laboratory results and more serious clinical outcomes. The consequences of viral infection require more consideration.

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