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Original Article

Clinico-radiological Profile and Outcome of Children with Viral Pneumonia admitted to Paediatric Intensive Care Unit in the pre COVID 19 period

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Abstract

Introduction: Viruses are common etiological agents of severe acute respiratory illness in under five children. Very few studies are available considering the profile of children with viral pneumonia admitted to paediatric intensive care unit (PICU) in our setting. Hence this study was done to describe the clinico- radiological profile and outcome of children diagnosed with viral pneumonia admitted to PICU.
Methods: This was a retrospective descriptive study done in the PICU of a tertiary care hospital in South India. The presenting clinical features, blood parameters, chest radiography findings, course during the hospital stay and outcome of children with viral pneumonia (RT- PCR Positive) admitted to PICU were studied.
Results: The aetiological profile of 28 children included - Influenza virus - 14 cases, Respiratory Syncytial Virus - 6 cases, Adeno virus - 4 cases, Human Boca virus - 2 cases, Human Rhino Virus - 1 case and Human metapneumo Virus - 1 case. Majority of children (50%) presented with severe respiratory distress. Predominant radiological picture included bilateral interstitial infiltrates followed by patchy alveolar consolidation. Eight children required mechanical ventilation. Complications included septic shock and MODS (n = 5), pneumothorax (n = 2), myocarditis (n = 2), pleural effusion (n = 1), ventilator associated pneumonia (n = 2) and pulmonary artery hypertension (n = 2). Mortality was observed in seven (25%) children. SpO_2 / FiO_2 ratio < 300, shock at admission, neutrophil leucocyte ratio > 2 and hypoalbuminemia were found to be significant predictors of mortality.
Conclusions: Malnutrition and iron deficiency anaemia were the common risk factors. Patchy alveolar consolidation is also a common radiological finding along with interstitial infiltrates. Hypoalbuminemia was a common finding among non-survivors.

Introduction

Pneumonia is the leading cause of mortality and morbidity in under five children.[1] Influenza and respiratory syncytial viruses are the common agents associated with viral pneumonia. Though majority of viral infections are benign and self-limiting, recently viruses are also implicated in the etiology of severe acute lower respiratory tract infections more often than previously reported.[2]

Early diagnosis is important in pneumonia not only to reduce morbidity and mortality

but also to avoid inappropriate use of antibiotics. Aetiological agents can be identified in only 30 - 50% of community acquired pneumonia.[2] RT-PCR (Reverse Transcription–polymerase Chain Reaction) assay of the nasopharyngeal / throat swab is a valuable test in the aetiological diagnosis of viral pneumonia. There is paucity of data on the profile of children with viral pneumonia admitted to the paediatric intensive care unit (PICU) in India.

The aim of this study is to describe the aetiological, clinical, radiological, laboratory features and outcome of children diagnosed with viral pneumonia by RT-PCR assay admitted to PICU.

Methods

This was a retrospective descriptive study conducted at the PICU of a tertiary care hospital. The study population included children between one month to five years of age admitted to PICU with viral pneumonia from January 2018 to June 2018. Viral pneumonia was defined as acute lower respiratory tract infection with the presence of abnormal chest X-ray and confirmed by RT-PCR assay of the throat swab/ nasopharyngeal aspirate.[2] Those children with suspect viral pneumonia but negative for RT-PCR assay were excluded. Those children with concomitant evidence of bacterial infection (Positive culture) at admission were also excluded. Ethical approval was obtained from the Institutional Ethics Committee.

Baseline demographic, clinical and laboratory data were collected from the patient file at the Medical Records Department and documented in the proforma designed for the study. Chest X-ray findings were documented and confirmed by a single designated radiologist. The severity of respiratory distress was assessed with PRESS (Paediatric Respiratory Severity Score) scoring system and classified into mild, moderate and severe respiratory distress. Treatment details were collected along with the length of PICU stay and total duration of hospital stay. Outcome was defined in terms of mortality and survival.

Chest X-ray was taken with Philips DR machine (resolution 800 ma). Abnormal findings in chest X-ray were classified into focal (Limited to a focus) and multifocal (More than one focus). Multifocal was further classified as unilateral or bilateral. X-ray finding was considered to be "diffuse" if there was extensive area involved bilaterally. The pattern of abnormal findings was further classified into four categories namely interstitial pattern (Reticular or peribronchial interstitial shadowing), patchy areas of consolidation, lobar consolidation or diffuse air space consolidation.

Obtained data was analyzed using the Statistical Package for Social Sciences (SPSS) V23.0. Descriptive data was expressed as frequencies and percentages. Mean and standard deviation were computed for the variables following normal distribution curve, while median and inter-quartile range were computed for non-parametric data. Fisher exact tests were used to test categorical variables. P value of < 0.05 was considered as statistically significant.

Results

During the study period, 42 children with suspected viral pneumonia were admitted to PICU. Twenty eight children with positive RT-PCR assay of the throat / nasopharyngeal aspirate were included in the study. The age of subjects ranged from two months to 44 months with a mean age of 20.4 months. Gender distribution was equal in the study population with a male : female ratio of 1:1.

The etiological profile of 28 children was as follows- Influenza virus - 14 cases (H1NI - eight cases, Influenza B virus - five cases, H3N2- One case), Respiratory Syncytial Virus (RSV) - six cases, Adeno virus (AdV) – four cases, Human Boca Virus (HBoV) - Two cases and one case each of Human Rhino Virus (HRV) and Human Meta-pneumo Virus (HMPV). Among 14 cases of Influenza, 10 cases occurred in the winter season (January to February).

The mean duration of symptoms prior to admission to PICU was 4.5 ± 1.88 days with a range of two to seven days. Fever, cough and respiratory distress were present in all children. One child with RSV pneumonia presented with stridor and croupy cough. In addition to the respiratory symptoms, three children with H1N1 pneumonia presented with loose stools and one child with Influenza B pneumonia presented with generalized tonic-clonic seizures. According to the assessment of respiratory distress done at admission by PRESS scoring system, seven (25%) children had mild respiratory distress, seven (25%) had moderate respiratory distress and 14 (50%) children had severe respiratory distress. Oxygen saturation of < 90% was found in 24 (85.7%) children. As arterial blood gas analysis reports were available in only eight children, we calculated SpO_2 / FiO_2 ratio in all children. Eight children had SpO_2 / Fi O_2 ratio of < 300 indicating need for mechanical ventilation. Features of shock were present in seven children at admission requiring inotropic or fluid support. Hepatomegaly was found in eight children. Associated comorbid conditions included malnutrition (n = 9), past history of recurrent wheeze (n = 3), pre-existing congenital heart disease (n = 3), pre-existing seizure disorder and developmental delay (n = 3) and cleft palate (n = 1).

Baseline demographic and clinical and laboratory characteristics are depicted in table 1. Anaemia was present in 14 (50%) children with a mean haemoglobin of 10.7 ± 1.52 g / dL. Leukocytosis was present in 12 (42.9%) children and leukocytopenia was present in three (10.7%) children while 13 (46.4%) children had normal leucocyte count. The mean total leucocyte count was 11.2 ± 6.94 x 10^9 cells / L (range 2.7-31.2x10^9 cells/L). Thrombocytopenia was present in 3 (10.7%) children and all 3 of them had mild thrombocytopenia. Serum C-reactive protein (CRP) was elevated in 5 (17.9%) children. Median CRP value was 6.35 mg/L (IQR 2.2-15.7). Elevated ESR was found in 6 (21.4%) children. Elevated liver enzymes were found in 10 (35.7%)

children. Elevated hepatic transaminases was a common finding in Influenza B pneumonia (Four out of five) and two cases of HBoV pneumonia. Hypoalbuminemia was present in 13 (46.4%) children.

Parameter (n = 28)	Influenza (n = 14)	RSV (n = 6)	AdV (n = 4)	HBoV (n = 2)	HMPV (n = 1)	HRV (n = 1)
Median age in years	2.2	1.2	1.1	3.3	2.1	0.9
Males & females	6 & 8	4 & 2	3 & 1	0 & 2	1 & 0	0 & 1
Median duration of illness in days	5.2	4.6	7.4	3.2	4.4	6.3
Presence of severe respiratory distress (n = 14)	6	3	2	2	0	1
Comorbidities -Malnutrition (n = 12) -Wheezing (n = 3) -Congenital heart disease (n = 3) -Seizure disorder (n = 3) -Cleft palate (n = 1)	 4 2 1 3 0	 4 0 0 0 0	 2 1 1 0 0	 2 0 0 0 1	 0 0 1 0 0	 0 0 0 0 0
Laboratory Parameters - Anaemia (n = 14) - Leucocytosis (n = 12) - Leucopenia (n = 3) - Thrombocytopenia (n = 3) - Elevated ESR (n = 6) - Elevated CRP (n = 5) - Raised AST & ALT (n = 10) - Hypoalbuminemia (n = 13)	 8 3 3 3 4 3 7 7	 4 5 0 0 1 1 2 3	 1 1 0 0 1 1 1 2	 1 1 0 0 0 0 0 0	 0 1 0 0 0 0 0 0	 0 1 0 0 0 0 0 1
Mechanical ventilation (n = 8)	3	2	2	0	0	1
Complications -Pleural effusion (n = 1) -Pneumothorax (n = 2) -Septic shock / MODS (n = 7) -Myocarditis (n = 2) -Ventilator Associated Pneumonia (n = 2) -Pulmonary artery hypertension (n = 2)	1 1 3 2 0 0	 0 0 1 0 0 0	 0 0 2 0 2 2	 0 0 0 0 0 0	 0 0 0 0 0 0	 0 1 1 0 0 0
Mortality (n = 7)	3	1		2	0	1

Table 1. Baseline demographic, clinical and laboratory characteristics of children with reference to aetiology

Most common abnormal finding in chest radiography was interstitial pattern observed in 14 (50%) children followed by patchy areas of consolidation in eight (28.6%), diffuse air space consolidation in four (14.3%) children and lobar consolidation in two (7.1%) children (Table 2). Lesions were bilateral in 24 (85.7%) children and unilateral in remaining four (14.3%) children. Lower lobes were frequently affected.

Other findings in chest x-ray included pneumothorax in two children and pleural effusion in one child. Radiological findings in viral pneumonia with respect to aetiology is described in table 2. Few of the chest x-rays are shown in figure 1.

Radiological Finding	Influenza (n = 14)	RSV (n = 6)	AdV (n = 4)	HBoV (n = 2)	HMPV (n = 1)	HRV (n = 1)
Interstitial pattern (n = 14)	7	3	2	2	0	0
Patchy consolidation (n = 8)	4	2	1	0	1	0
Lobar consolidation (n = 2)	1	1	0	0	0	0
Diffuse air space consolidation (n = 4)	2	0	1	0	0	1

Table 2. Radiological findings in children with viral pneumonia based on aetiology

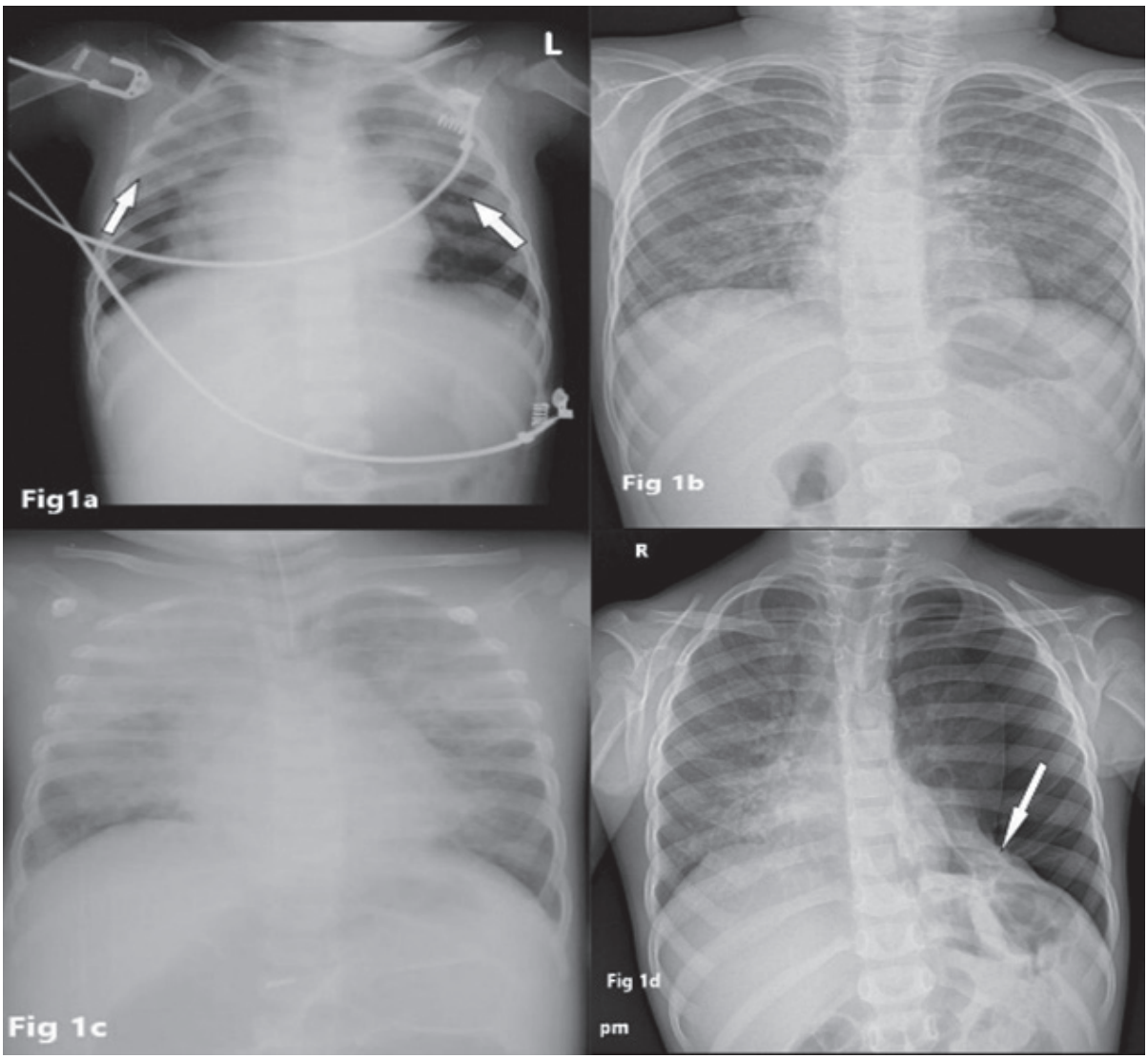

Figure 1. Chest x-ray showing 1a. Bilateral patchy consolidation of upper and middle zone (white arrow). 1b. Bilateral peribronchial interstitial shadowing. 1c. Bilateral diffuse air space opacities with hyperinflation. 1d. Left sided tension pneumothorax with mediastinal shift and collapsed border of left lung (arrow); patchy consolidation in lower lobe of right lung.

All children required oxygen supplementation and inhaled bronchodilators. Awaiting RT-PCR assay report all children were empirically started on oral Oseltamivir. Oseltamivir was continued for five to seven days in children positive for Influenza. Two children with severe RSV pneumonia and two children with Adenoviral pneumonia were treated with oral Ribavirin. Eight children were treated with broad spectrum intravenous antibiotics to prevent secondary bacterial infection. Two children required HFNC (High Flow Nasal Cannula) and eight (28.6%) children required mechanical ventilation (Two H1N1, two RSV, one Influenza B, two Adenovirus, one HRV). Mean duration of PICU stay was 8.2 ± 4.02 days (Range three to 19 days). Two children with H1N1 and one child with Adenovirus pneumonia required prolonged ICU stay (> 10 days). Complications included septic shock and MODS (Multi organ dysfunction syndrome) (n = 7), pneumothorax (n = 2), myocarditis (n = 2), ventilator associated pneumonia (VAP) (n = 2), pulmonary arterial hypertension (PAH) (n = 2) and pleural effusion (n = 1). Mortality was observed in seven (25%) children (Two H1N1, two Adenovirus, one RSV, one Influenza B, one HRV)

Parameter	Survivors (n = 21)	Non-survivors (n = 7)	OR [95% CI]	P value
Age < 1 year (n = 14)	10	4	0.69 [0.08, 5.24]	*1.0
Malnutrition (n = 12)	10	2	2.2 [0.28, 28.20]	*0.66
SpO_2 at admission < 90% (n = 24)	10	14	0.52 [0.0042, 3.64]	*0.312
SpO_2 / FiO_2 < 300 (n=8)	1	7	0.01 [.00017, 0.18]	*0.00005
Shock at admission (n = 7)	2	5	0.05 [0.0028, 0.53]	*0.0038
Anaemia (n = 14) Mean haemoglobin (g/dL)	11 10.59 ± 1.54	3 11.00 ± 1.57	1.44 [0.19, 12.44]	*1.0 #0.55
Leukocytosis (n=12) Median TLC (x10^9 cells/L) (IQR)	8 7700 (5600; 16900)	4 11,700 (6600; 15800)	0.47[0.05, 3.64]	*0.41 ##0.71
NLR > 2 (n = 9) Median NLR (IQR)	2 0.85 (0.7; 1.8)	7 2.00 (1.5; 6.7)	0.062 [0.004,0.52]	*0.0027 ##0.0257
CRP > 30 mg / L (n = 5) Median CRP (IQR)	3 6.2 (2.20; 15.12)	2 8.2(2.54; 22.05)	0.43[0.03, 6.50]	*0.57 ##0.67
Liver dysfunction (n = 10)	7	3	0.67 [0.085, 5.93]	*0.674
Hypoalbuminemia (n = 13) Mean serum albumin ± SD	7 3.42 ± 0.63	6 2.96 ± 0.40	0.09[0.0017, 0.97]	*0.0286 #0.08

Table 3. Predictors of mortality in children with viral pneumonia

*Fisher exact test, #Independent Sample T-test, ## Mann-Whitney U test OR [95% CI]- Odds ratio, 95% Confidence Interval

Common predictors of mortality were compared between survivors and non-survivors (Table 3). It was found that malnutrition and anaemia were predominantly associated with mortality risk (Odds ratio of 2.2 and 1.44 respectively). Presence of shock at admission and SpO_2 / FiO_2 ratio of < 300 were found to be significant predictors (p value 00038 and < 0.001); Fisher exact test). Among laboratory parameters, NLR (Neutrophil lymphocyte ratio) of > 2 and hypoalbuminemia were significantly associated with mortality (p value 0.027 and 0.028 respectively; Fisher exact test).

Discussion

Viruses play a significant role in the aetiology of community acquired pneumonia (CAP) in children. The present study included 28 children diagnosed with viral pneumonia admitted to PICU. Majority of the study population were infants (50%). Children were classified into six groups based on aetiology. Influenza viruses were the most common pathogens (50%) followed by RSV. Similar findings were observed in a retrospective study by Guo W et al.[3] In majority of studies from India, RSV was the most common aetiological agent.[4,5] In a study done by Mishra P et al in Eastern India, HRV was the commonest pathogendetected followed by RSV and Para influenza viruses.[6] HMPV was most commonly detected in children with severe respiratory infection in a study by Malhotra B et al.[7] In most of the studies it is well established that outbreaks occur mostly during winter season followed by rainy season.[4-7] We observed seasonal preponderance in the Influenza group.

PRESS score was used to classify the severity of respiratory distress at admission. This scoring system was designed in Japan to grade the severity of respiratory illness mainly related to viral pneumonia.[8] It includes objective assessment by the clinician in contrast to WHO staging of severe pneumonia and very severe pneumonia. As the study population included only those admitted to PICU, majority of children (50%) had severe respiratory distress. Twenty four children were found to be hypoxic. Thus hypoxia disproportionate to respiratory distress is commonly observed in viral pneumonia.

Previous studies have observed various risk factors for viral pneumonia including chronic wheeze, malnutrition, anaemia, immunodeficiency, prematurity, smokers in family, overcrowding, attending day care centre etc.[9-11] We found malnutrition and anaemia in 12 (42.8%) and 14 (50%) children respectively. Three children had positive history of pre-existing recurrent wheeze and

three children had congenital heart disease.

The role of routine haematological tests in differentiating viral and bacterial community pneumonia has been extensively studied.[12,13] Leukocytosis, elevated ESR and CRP usually favour bacterial aetiology. However, according to a study done by Virkki R et al, it was found that the finding of leukocytosis (WBC > 15.0 X 10^9 / l) and increased ESR > 30 mm / hr was similar in both bacterial and viral pneumonia (48% v 47% and 66% v 60%, respectively). However, the differences in the CRP levels between the two groups were significant at the selected levels of > 40 mg / l (p = 0.004) and a CRP concentration of > 80 mg / l significantly predicted bacterial pneumonia in the younger age group (< 2 years).[13] In the present study, leucocytosis was present in 12 (42.9%) children and CRP was elevated in five (17.9%) children. Elevated ESR was found in only six (21.4%) children. We found elevation of hepatic transaminases in 10 children, more commonly in the Influenza group. Few studies have also reported asymptomatic elevation of transaminases in Influenza pneumonia.[14]

Chest X-ray findings are traditionally classified as lobar pneumonia, bronchopneumonia and interstitial pneumonia. It is well known that lobar pneumonia is commonly found in bacterial pneumonia while interstitial opacities are commonly found in viral pneumonia.[13,15] However, in a study by Guo W et al, chest X-ray findings of 210 children with viral pneumonia was retrospectively analyzed. It was found that the predominant radiological finding was bilateral patchy areas of consolidation (63.4%) followed by interstitial opacities (15.7%), diffuse air space consolidation (13.8%) and lobar consolidation (7.1%).[3] In contrast, we found interstitial pattern in 14 (50%) children followed by patchy areas of consolidation in eight (28.6%), diffuse air space consolidation / ARDS in four (14.3%) and lobar consolidation in two (7.1%) children. In this study, a single radiologist confirmed the findings. Hence this is one of the drawback of our study as it is better to have X-ray findings confirmed by two separate radiologists where one can account for inter-observer variability.

Management mainly involves providing supportive measures and prevention of secondary bacterial infection. Antiviral agents include Oseltamivir for Influenza viruses and Ribavirin for RSV. In addition, IV Immunoglobulin has been tried in children with severe adeno viral pneumonia.[16] Common complications associated with viral pneumonias include acute respiratory failure requiring mechanical ventilation, pneumothorax, pleural effusion, secondary bacterial infection, sepsis, MODS and myocarditis. In the present study, eight (28.6%) required mechanical ventilation. Septic shock and MODS was observed in seven children. Other complications observed were pneumothorax (n = 2), ventilator associated pneumonia (n = 2), myocarditis (n = 2) and pleural effusion (n = 1). We also observed two children developing pulmonary arteries hypertension during second week of illness.

Mortality was observed in seven (25%) children. Studies have described predictors of morbidity and mortality in children with pneumonia. Few of the common predictors include younger age (< one year), malnutrition, anaemia, presence of shock, leukocytosis, elevated NLR, SpO_2 / SpO_2 < 200 and hypoalbuminaemia.[17-19] In a study done by Shi J et al, septic shock and liver dysfunction were independent risk factors for mortality in children with Adeno virus pneumonia.[20] According to a study done by Sanz F et al on patients with severe pneumonia, it was found that estimation of PaO_2 derived from SpO_2 is accurate enough for initial oxygenation assessment.[21] In this study, shock at admission, SpO_2 / FiO_2 ratio of < 300, NLR > 2 and hypoalbuminemia were found to be predictors of mortality.

The clinical presentation, radiological features, severity of illness and outcome of individual case with respect to aetiology has been described in this study. The study also stresses the importance of risk factors for pneumonia such as anaemia and malnutrition. Hypoalbuminaemia was also a predictor of mortality. Hence improvement of nutritional status and correction of anaemia play a vital role in prevention of pneumonia and its complications. However, the descriptive nature of the study and data collection performed retrospectively with small sample size account for its limitations.

Conclusions

Viral pneumonia is an important cause of morbidity and mortality in PICU. It is important to consider viral etiology in a rapidly progressing pneumonia with radiological picture and hypoxemia disproportionate to clinical features, in the absence of laboratory markers of bacterial infection. Further prospective observational studies in large population are needed to estimate the severity and outcome of viral pneumonia in PICU.

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