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Clinical Course and Outcome of Laboratory-Confirmed Severe Respiratory Syncytial Virus and Influenza A Virus in Immunocompetent Admitted Patients at Children Hospital PIMS Islamabad

Maryam Naseer[1], Nadia Waheed[2], Muqaddar Shah[3], Rehmana Waris[4], Ayesha Abdul Razzaq[5], Muhammad Jawad[6]

Department of Paediatric Medicine, Children Hospital, PIMS, Islamabad

ABSTRACT

Objective: To determine the presentation, clinical course, complications, response to treatment, and outcome of children hospitalized with respiratory tract infections caused by respiratory syncytial virus (RSV) and Influenza A virus (H1N1) in a tertiary care hospital of Islamabad.

Methodology: A prospective cross-sectional study was conducted in the West Medical ward, Children Hospital, PIMS, Islamabad. A total of 50 patients between the ages of 0 to 13 years admitted with an acute respiratory illness and having positive PCR for RSV and Influenza A (H1N1) between August 2022 to March 2023 were included in this study. All data regarding presentation, clinical course, complications, treatment, and outcome were recorded in the proforma. Descriptive analysis was done.

Results: The median age of presentation of RSV infection was 0.30(0.30) years, and of H1N1 was 1.40(3.65) years. Almost 50% of affected patients were below 3 months age. Multisystem involvement in the form of myositis, hepatitis, encephalitis, and carditis was more common in the RSV group, while respiratory complications (pneumothorax, lung consolidation/collapse) were more common in the H1N1 group. Mean C-reactive protein (CRP) and duration of hospital stay of H1N1 positive patients were twice as compared to RSV infected patients.

Conclusion: Both RSV and H1N1 have become more invasive and caused more severe complications as compared to the pre-COVID-19 era. It is high time to increase awareness regarding the RSV and Flu vaccine among children in this post-COVID-19 era.

Keywords: Acute Respiratory Illness, Antiviral, Lung consolidation, Polymerase Chain Reaction (PCR), Pneumothorax.

Authors' Contribution:
[1,2]Conception; Conception of the work idea, data collection, [4-6]analysis and interpretation, drafting the manuscript, [3]reviewing and final approval.

Correspondence:
Dr Maryam Naseer
Medical Officer Paeds Medicine
Children Hospital, PIMS, Islamabad
Email: maryamnaseer177@gmail.com

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Introduction

Respiratory tract infections are one of the leading causes of hospitalization in infants and young children. Viruses account for 40-50 % of these hospitalizations in developing countries.[1] Among viruses, respiratory syncytial virus (RSV) and Influenza viruses are the leading causes of hospitalization in children.[2] The average hospitalization rate attributed to RSV and Influenza infection is 2.5-9.9 and 1-5 per 100 children, respectively.[3,4] Many studies have been conducted in developing countries on assessing the disease burden associated with RSV and influenza-associated hospitalizations among children.

RSV is a ribonucleic acid (RNA) virus of the Pneumoviridae family that spreads through respiratory droplets and direct contact with contaminated surfaces.[5] It mostly affects children during the winter and autumn seasons. RSV is responsible for flu-like

illness, 50 % of pneumonia and 40-90 % of bronchiolitis admissions among children below 2 years of age.[6] Influenza is an RNA virus that belongs to the Orthomyxoviridae family. It is responsible for flu-like illness and pneumonia among young children, mostly during the fall and winter seasons. High-risk patients may develop complications like myocarditis, myositis, renal failure, encephalitis, sepsis, and even death.

In Pakistan, very few studies have been conducted on the prevalence of RSV and influenza-related hospitalizations in children. Unfortunately, no studies have been conducted on clinical course, outcome, and complications (pneumothorax, pneumo mediastinum, pleural effusion, myositis, carditis, hepatitis, and encephalitis) related to invasive RSV and influenza-associated hospitalization. There has been a major change in prevalence, clinical presentation, and complications related to RSV and Influenza virus in post post-Coronavirus disease 2019 (COVID-19) era, which has not been studied yet in Pakistan.

The purpose of our study is to determine the presentation, clinical course, complications, response to treatment, and outcome of children hospitalized with respiratory tract infections caused by RSV and Influenza virus in a tertiary care hospital in Islamabad. We would also determine if early detection and early treatment can change the course of illness among these children. This information will be useful for clinicians in defining the Influenza and RSV management program and will help in the prevention of the spread of this deadly infection.

Methodology

This was a prospective cross-sectional study conducted in the West Medical Ward of the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad, after obtaining approval from the institutional ethical review board. All patients aged 0 to 13 years who were admitted with an acute respiratory illness between August 2022 to March 2023 were included. The inclusion criteria were children within the specified age range who presented with severe acute respiratory illness (SARI), defined by the World Health Organization (WHO) as an acute respiratory infection with symptoms of fever (>38 °C) and cough, with onset within the last 10 days requiring hospitalization, and who tested positive for influenza or respiratory syncytial virus (RSV) by RT-PCR.

After confirming eligibility and receiving informed consent from the parent or guardian, demographic and clinical information about the current illness was recorded. A throat, nasal, or nasopharyngeal swab was obtained and immediately transported to the research laboratory in the National Institute of Health (NIH), Islamabad, for testing of Influenza and RSV virus using a real-time reverse transcriptase polymerase chain reaction (PCR) detection system. 50 patients whose PCR came out to be positive for RSV or Influenza virus were included in the study. All data, including clinical manifestations, laboratory parameters, clinical course, outcome, and complications were recorded on a pre-designed proforma. Statistical analysis was performed in SPSS version 22.

Results

Among all the patients who presented with acute respiratory illness, viral PCR came out to be positive in 28% of patients. Among these, 34(68%) patients were RSV positive, 14(28%) were Influenza type A(H1N1) positive, 1(2%) was Influenza type B positive and 1(2%) patient was positive for both RSV and Influenza type A(H1N1) simultaneously. The median age of presentation of RSV infection was 0.30(0.30) years, and of H1N1 was 1.40(3.65) years. In our study, 14 out of 15 patients who turned out to be Influenza virus positive were infected with the Influenza A (H1N1) strain, so our study is mainly focused on the clinical presentation of RSV and H1N1 virus. Almost 50% of affected patients were below 3 months age.

In this study, males were more commonly infected as compared to females. Out of 34 patients who came out to be RSV positive, 24(48%) were males and 10(20%) were females, while in the H1N1 group, 11(22%) were males and 3(6%) were females. 1 patient affected with Influenza type B and 1 with co-infection of RSV and H1N1, both were males.

Fever was present in all patients, but high-grade spiking fever was present in 20(40%) RSV-positive and 12(24%) H1N1-positive patients, respectively. Gastrointestinal symptoms in the form of vomiting were the presenting complaint in 4(8%) RSV-positive and 5(10%) H1N1-positive patients, while diarrhea was present in 1(2%) RSV-positive patients and 3(6%) H1N1-positive patients, respectively. Central nervous system involvement in the form of fits and altered sensorium was present in 5(10%) RSV-positive

patients and 6(12%) H1N1-positive patients, respectively. Seizures and low GCS were also present in 1 patient having Influenza type B infection and 1 patient having co-infection with RSV and H1N1 virus. Cerebrospinal fluid proven encephalitis was present in 2(4%) RSV-positive, 1(2%) H1N1-positive, and 1(2%) patient who was both RSV and H1N1 positive, respectively. Maculopapular rash involving the whole body was the presenting complaint in 2(4%) RSV-positive and 1(2%) H1N1-positive patients, respectively.

Respiratory symptoms in the form of cough and breathing difficulty were present in all patients. Bronchiolitis and pneumonia were the most common causes of these symptoms. Among these, 5(10%) H1N1 positive patients developed lung collapse/consolidation followed by pneumothorax, and 4(8%) among them required ventilatory support. In contrast, only 1(2%) RSV-positive patient developed lung collapse/consolidation followed by pneumothorax.

Acute hepatitis with raised ALT was present in 8(16%) RSV-positive patients and 7(14%) H1N1-affected patients, respectively. Median alanine transaminase (ALT) of RSV-positive and H1N1-positive patients was 34.00(8.75) U/L and 42.50(97)U/L, respectively. Myocarditis with raised cardiac enzymes was present in 7(14%) RSV-positive, 4(8%) H1N1-positive, and 1(2%) influenza type B-positive patients, respectively. Myositis with raised CPK was present in 4(8%) RSV-positive and 1(2%) H1N1-positive patients, respectively.

Mean Total leukocyte count (TLC) of RSV positive patients was $13.51\pm7.47\times10^9$/L with 49.62±14.45% neutrophils and 41.37±13.76% lymphocytes, while TLC of H1N1 positive patients was $12.67\pm11.37\times10^9$/L with 57.23±21.45% neutrophils and 34.60±17.99% lymphocytes. Median C-reactive protein (CRP) of RSV-positive and H1N1-positive patients was 27.05(17.40) mg/dl and 61.00(99.75) mg/dl. Median alanine transaminase (ALT) of RSV-positive and H1N1-positive patients was 34.00(8.75) U/L and 42.50(97.00) U/L, respectively.

7(14%) patients who were infected with RSV infection had some underlying illness, while 9(18%) patients with HINI infection had some underlying illness. 1(2%) patient infected with Influenza type B and 1(2%) having co infection with RSV and H1N1 simultaneously were having some underlying illness. Most of these patients were having some underlying cardiovascular, central nervous system, or respiratory system illness. Mean duration of oxygen dependency was 5.47±3.01 days and 12.78±7.07 days in RSV-positive and H1N1-positive patients, respectively. Mean duration of hospital stay for RSV positive patients was 7.85±3.08

Table I: Demographic characteristics of patients (n=50)

Parameter	RSV N (%)	Influenza A (H1N1) N(%)	Influenza B, N(%)	Both (H1N1 and RSV) N(%)
Age groups				
<3 months	18(36)	3(6)	1(2)	
3 months-1 years	15(30)	3(6)		
1-5 years	0	7(14)		
>5 years	1(2)	1(2)		1(2)
Gender				
Male	24(48)	11(22)	1(2)	1(2)
Female	10(20)	3(6)		
Clinical presentations				
Fever	20(40)	12(24)		
Cough	29(58)	8(16)		
Bronchopneumonia	18(36)	8(16)	1(2)	1(2)
Lung collapse/ consolidation/ pneumothorax	1(2)	5(10)		
GIT symptoms	8(16)	5(10)	1(2)	
CNS symptoms	5(10)	6(12)	1(2)	1(2)
CVS symptoms	7(14)	4(8)	1(2)	
Comorbid				
CSF findings (encephalitis)	2(4)	1(2)		1(2)
Hepatitis	8(16)	7(14)	1(2)	
Myositis	4(8)	1(2)		
Underlying illness	7(14)	9(18)	1(2)	1(2)
Mortality	2(4)			1(2)

days, and for H1N1 positive patients was 14.85±8.17 days.

2(4%) H1N1 positive and 1(2%) patient having co infection with RSV and H1N1 expired during the course of illness. All these patients had some underlying illness. No specific post-recovery complications were noted in any patient. Response to antivirals was good. Early initiation of antiviral therapy was associated with a good prognosis.

Table II: Laboratory findings.

Parameters	Mean±SD/ Median (IQR)	
	RSV	Influenza A(H1N1)
Age (years)	0.30(0.30)	1.40(3.65)
TLC (10^3/µL)	13.51±7.47	12.67±11.37
CRP (mg/L)	17.4(27.05)	61(99.75)
Neutrophils (%)	49.62±14.45	57.23±21.45
Lymphocytes (%)	41.37±13.76	34.60±17.99
ALT	34.00(8.75)	42.50(97)
Duration of oxygen dependency(days)	5.47±3.01	12.78±7.07
Duration of hospital stay(days)	7.85±3.08	14.85±8.17

Discussion

In our study, children of both groups presented with symptoms involving almost all body systems. Central nervous system (CNS) involvement in the form of fits and altered sensorium was present in 5(10%) RSV-positive and 6(12%) H1N1-positive patients, which is comparable to another study in which 1 in 9 (11.1%) patients admitted with Influenza virus infection had CNS involvement.[8]

10% of H1N1-affected patients developed lung collapse/consolidation followed by pneumothorax and required ventilatory support and intensive care, but only 1 RSV-affected patient required ventilatory support and ICU care due to multi-organ involvement. This is in contrast to other studies in which comparable rates of 3.1 and 4.3% of ICU admissions associated with RSV and Influenza have been reported, respectively.[9] In another study, no child with Influenza was admitted to the ICU, while 3.6% of RSV-infected children required it, and no death was reported among children in both groups.[10]

Cardiac involvement in the form of myocarditis was present in 14 and 8% of RSV and H1N1-affected patients, respectively. Myositis, hepatitis were also noted in both groups of patients, but were more common in RSV-affected patients.

The mean duration of stay of H1N1-affected patients was twice as compared to RSV patients, and it was in contrast to another study in which there was no significant difference in the mean duration of hospital stay of both groups.[9] A longer duration of hospitalization of RSV-infected patients has also been reported previously.[11]

RSV infection was mostly present in healthy children, with only 14% having some underlying illness, while 18% of patients affected with H1N1 had some underlying CNS, CVS, or respiratory tract illness. This is in contrast to another study in which there was a 5-fold increased risk of having RSV infection in patients with some underlying illness.[12] In another study, there was no significant difference in underlying comorbidities between the groups.[13] Mean duration of stay and oxygen dependency of H1N1 patients was double as compared to RSV-affected patients.

Laboratory parameters only had a supportive role in determining the severity of illness. Mean CRP value of H1N1-infected patients was thrice as compared to RSV patients. H1N1-infected patients had a longer duration of illness with raised inflammatory markers and a high rate of mortality, while RSV-affected patients had a less severe course of illness but with multi-organ involvement. All multisystem involvement was 100% reversible.

The case fatality rate of our study was 14% which was higher than compared of another study.0[14] All of them had some underlying illness. Increased incidence of mortality may be due to a sudden rise in RSV and Influenza infection in post post-COVID-19 era.

There was no difference in the overall antibiotic utilization between RSV and influenza-affected patients. Septic appearance on admission and raised inflammatory markers were associated with increased use of antibiotics in both groups. Vigorous use of antibiotics did not change the course of the illness of disease.

There are multiple antivirals available for RSV and influenza-affected patients with severe illness. In our study, patients affected with severe RSV infection and multi-organ involvement were treated with oral ribavirin for 7 to 10 days (due to non-availability of aerosolized ribavirin). Oral ribavirin is safe, cost-effective, and easier to administer compared to aerosolized ribavirin. Those affected with severe Influenza with multi-organ

involvement were treated with oral oseltamivir for 10 to 14 days. Early initiation of treatment decreased the severity and duration of illness, but focused studies need to be conducted on the use of these antivirals.

Conclusion

Both RSV and H1N1 have become more invasive and caused more severe complications as compared to pre pre-COVID-19 era. H1N1 was associated with increased risk of developing deadly respiratory complications, increased duration of illness, and increased duration of oxygen therapy, while RSV is more associated with multisystem involvement. It is highly suggested to include RSV and Influenza vaccines in the EPI program. It is high time to increase awareness regarding the RSV and Flu vaccine among children in this post-COVID-19 era. Introduction of the RSV vaccine among pregnant women can also be very effective in preventing infection among infants, as most RSV infections occur in infants.

References

1. Tregoning JS, Schwarze J. Respiratory viral infections in infants: causes, clinical symptoms, virology, and immunology. Clin Microbiol Rev. 2010;23(1):74-98. https://doi.org/10.1128/CMR.00032-09
2. Shi T, McAllister DA, O'Brien KL, Simoes EAF, Madhi SA, Gessner BD, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet. 2017;390(10098):946-58. https://doi.org/10.1016/S0140-6736(17)30938-8
3. Nair H, Brooks WA, Katz M, Roca A, Berkley JA, Madhi SA, et al. Global burden of respiratory infections due to seasonal influenza in young children: a systematic review and meta-analysis. Lancet. 2011;378(9807):1917-30. https://doi.org/10.1016/S0140-6736(11)61051-9
4. Hall CB, Weinberg GA, Blumkin AK, Edwards KM, Staat MA, Schultz AF, et al. Respiratory syncytial virus-associated hospitalizations among children less than 24 months of age. Pediatrics. 2013;132(2):e341-8. https://doi.org/10.1542/peds.2013-0303
5. Ogra PL. Respiratory syncytial virus: the virus, the disease and the immune response. Paediatr Respir Rev. 2004;5 Suppl A:S119-26. https://doi.org/10.1016/S1526-0542(04)90023-1
6. Homaira N, Oei JL, Mallitt KA, Abdel-Latif ME, Hilder L, Bajuk B, et al. High burden of RSV hospitalization in very young children: a data linkage study. Epidemiol Infect. 2016;144(8):1612-21. https://doi.org/10.1017/S0950268815003015
7. World Health Organization. Case definitions for ILI and SARI [Internet]. Available from: https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/case-definitions-for-ili-and-sari
8. Ghosh U, Bharathy RVN, Prasad DJH, Moorthy M, Verghese VP. An eight-year profile of children with influenza A(H1N1) in a large hospital in India. J Trop Pediatr. 2021;67(4):fmab084. https://doi.org/10.1093/tropej/fmab084
9. McMorrow ML, Tempia S, Walaza S, Treurnicht FK, Moyes J, Cohen AL, et al. The role of HIV in influenza- and respiratory syncytial virus-associated hospitalizations in South African children, 2011-2016. Clin Infect Dis. 2018;67(10):1588-96. https://doi.org/10.1093/cid/ciy532
10. Amini R, Gilca R, Boucher FD, Charest H, De Serres G. Respiratory syncytial virus contributes to more severe respiratory morbidity than influenza in children <2 years during seasonal influenza peaks. Infection. 2019;47(4):595-601. https://doi.org/10.1007/s15010-019-01287-5
11. Resch B, Eibisberger M, Morris N, Müller W. Respiratory syncytial virus- and influenza virus-associated hospitalizations in infants less than 12 months of age. Pediatr Infect Dis J. 2011;30(9):797-9. https://doi.org/10.1097/INF.0b013e318215cf3e
12. Pellegrinelli L, Galli C, Bubba L, Seiti A, Anselmi G, Primache V, et al. Respiratory syncytial virus in pediatric influenza-like illness cases in Lombardy, Northern Italy, during seven consecutive winter seasons (from 2014-2015 to 2020-2021). Influenza Other Respir Viruses. 2021 Dec 17. https://doi.org/10.22541/au.163508928.85347830/v1
13. Papan C, Willersinn M, Weiß C, Karremann M, Schroten H, Tenenbaum T. Antibiotic utilization in hospitalized children under 2 years of age with influenza or respiratory syncytial virus infection: a comparative, retrospective analysis. BMC Infect Dis. 2020;20(1):598. https://doi.org/10.1186/s12879-020-05336-5
14. Bont L, Checchia PA, Fauroux B, Figueras-Aloy J, Manzoni P, Paes B, et al. Defining the epidemiology and burden of severe respiratory syncytial virus infection among infants and children in Western countries. Infect Dis Ther. 2016;5(3):271-98. https://doi.org/10.1007/s40121-016-0123-0