American Journal of Clinical Microbiology and Antimicrobials

Research Article
Published: 23 Aug, 2021

Respiratory Syncytial Virus and Influenza Virus Co-Infection in the Era of COVID-19 Pandemic

Prashant Patil[1], Santosh Karade[1], Sourav Sen[2] and Pratik Thosani[1]*

[1]Department of Microbiology, Armed Forces Medical College, India

[2]Department of Microbiology, Symbiosis Medical College for Women, India

Abstract

Background: Respiratory Syncytial Virus (RSV), a known viral pathogen of pediatric age group is now an emerging cause of severe respiratory illness in adults. Human Influenza virus is the known cause of morbidity and mortality in adults. In the current setting of COVID-19 pandemic, RSV, and influenza viral infections in cases of Severe Acute Respiratory Infections (SARI) may be overlooked. Both these viral infections have similar clinical presentation and needs to be differentiated for appropriate management.

Materials and Methods: In this cross-sectional pilot study, nasopharyngeal swab samples from individuals in western region of Maharashtra state, India with severe acute respiratory infections were tested for SARS-CoV-2, RSV-A, RSV-B, Human Influenza A and B viruses by multiplex Real-Time Polymerase Chain Reaction (RT-PCR).

Results: Multiplex PCR of total of 100 consecutive samples of SARI were successfully processed during the study period between June 2020 to September 2020. RT-PCR showed genomic target detection for SARS-CoV-2, RSV, and Influenza virus in a total of 35, 22 and 03 samples, respectively. Prevalence of RSV-B (19%) was higher as compared to RSV-A (3%).

Conclusion: RSV infection in adults cannot be under rated in current scenario. The study highlights the importance of identifying other respiratory pathogens for specific management during current COVID-19 pandemic.

Keywords: SARS-CoV-2; H1n1; Real-Time PCR; Acute respiratory infection

OPEN ACCESS

Correspondence:
Sourav Sen, Professor and Head, Department of Microbiology, Symbiosis Medical College for Women, Lavale, Mulshi Rd, Pune, Maharashtra, 412115, India, Tel: 0000-0001-9117-2235; E-mail: sensourav@hotmail.com

Received Date: *12 Jul 2021*
Accepted Date*: 18 Aug 2021*
Published Date*: 23 Aug 2021*

Citation:
Patil P, Karade S, Sen S, Thosani P. Respiratory Syncytial Virus and Influenza Virus Co-Infection in the Era of COVID-19 Pandemic. Am J Clin Microbiol Antimicrob. 2021; 4(1): 1053.

Introduction

Global pandemic response to Severe Acute Respiratory Syndrome associated virus - 2 (SARS-CoV-2) infections has shifted the focus from other common respiratory viral illnesses. Respiratory Syncytial Virus (RSV) infection is still an important cause of hospitalization in children, as it causes acute bronchiolitis, and pneumonia [1]. Whereas influenza viral pneumonia also causes morbidity and mortality in current setting. There is need to study other RSV and Influenza viral co-infections in cases with acute respiratory illnesses in the present scenario of COVID-19 pandemic.

Respiratory Syncytial Virus A and B (RSV-A and RSV-B) are emerging pathogen causing respiratory illness in adults and responsible for approximately 64 million cases and 160,000 deaths globally [2,3]. Human RSV is an enveloped, single stranded, negative sense RNA virus of order *Mononegavirales*, family *Paramyxoviridae*, and subfamily *Pneumovirinae* [4]. Influenza virus belongs to the family *Orthomyxoviridae* with seven genera or types, of which Influenza A and influenza B are common. These are enveloped RNA virus with segmented, single stranded, negative sense genome. Infection with influenza can cause of spectrum of illnesses from mild flu like illness to severe pneumonia and acute respiratory distress syndrome, which is at time clinically indistinguishable from COVID-19 [5].

First reported in Wuhan city, China, the emergence, and global spread of SARS-CoV-2 infection has turned out to be a major public health and economic challenge [6]. For early identification and initiating isolation measures Government of India initiated "Test, Treat and Trace" strategy by operationalizing number of laboratories for diagnosing SARS-CoV-2 infection [7]. As SARS-CoV-2, RSV and human influenza virus have common mode of transmission and similar clinical presentation, the presence of co-infection cannot be ruled out. Therefore, in this pilot study we assessed presence of SARS-CoV-2, RSV and Influenza co-infection in adults presenting with Severe

Acute Respiratory Infections (SARI) in western Maharashtra, India.

Material and Methods

This cross-sectional study was carried out at ICMR approved SARS-CoV-2 diagnostic laboratory of Western Maharashtra, India. The target population included all individuals presented to respiratory out-patient and in-patient department for COVID-19 screening. The study population included all cases of Severe Acute Respiratory Infection (SARI). A case of SARI was defined as an individual presented with fever and at least one symptom of respiratory disease, such as cough, shortness of breath, warranting hospitalization. Children, pregnant females, and individuals with immune-compromised state were excluded from study. The sample consisted of Nasopharyngeal (NP) swab collected in viral transport medium under appropriate biosafety conditions. All NP swabs were processed for SARS-CoV-2 reverse transcription Real-Time Polymerase Chain Reaction (RT-PCR). Additionally, all SARI cases were all subjected to real-time PCR for genomic detection of RSV A, RSV B, Human influenza virus A and Human influenza virus B. In view of limited resources, a convenient sample size of 100 cases of SARI was considered in this pilot study.

RNA extraction was performed by silica column method using Qiagen RNeasy Mini kit as per manufacturer guidelines [8]. Extracted RNA was then subjected to RT-PCR using Super Script III Platinum Invitrogen one step RT-PCR kit [9,10]. RT PCR for detection of SARS-CoV-2 was performed using primers directed against envelope (E-Sarbeco) and open reading frame (HKU-ORF1b) specific for Wuhan SARS coronavirus [11,12]. Primers targeting N gene were chosen for detection of RSV A and RSV B as described previously [9]. Primers targeting M gene for Influenza A and NS gene for Influenza B were chosen for detection [10]. A known positive control for each target was used for validation of RT PCR assay. Primer targeting human Ribonuclease P (RNAaseP) was included for each sample as internal control.

Written informed consent was obtained from study participants. All individuals were identified by a unique identification number and the study was approved by Institutional Ethics committee.

Results

A total of 18,163 NP swabs were tested for SARS-CoV-2 RT-PCR between June 2020 to September 2020 with a positivity rate of 28.9%. Multiplex PCR of total of 100 consecutive samples of SARI during study period were successfully processed for RSV and Human influenza virus. The median age of study population was 30 years and 65% of them were male. The clinico-demographic profile of study population is shown in Table 1. Genomic targets for SARS-CoV-2, RSV and Influenza virus were detected in a total of 35, 22 and 03 samples, respectively. SARS CoV-2 and RSV co-infection was seen in 5% (Figure 1). The prevalence of RSV B (19%) was higher than RSV A (2%). Influenza and SARS CoV-2 co-infection was not detected, Influenza A was detected in 03 samples and all of them were pandemic 2009 H1N1 subtype. In this study Human Influenza B infection was not detected in individuals with SARI.

Discussion

With over 10.6 million cases of COVID-19 till January 2021, India is one of the three leading countries with SARS-CoV-2 infection [13]. It can cause mild flu like illness to severe pneumonia with acute respiratory distress syndrome and multi organ dysfunction. Although uncommon, co-infections with other viruses and bacteria are reported in COVID-19 [14]. Although, RSV predominantly infects children, there is growing evidence of increase in infection rate in adults also [2]. Humans are the only natural host for RSV with an incubation period of 3 to 5 days. RSV initially infects the nasopharynx, and then spreads to the lower respiratory tract [15]. It can cause mild upper respiratory tract infection to severe pneumonia. Whereas the incubation period of influenza virus infection is 1 to 4 days. It replicates in the upper respiratory tract and can spread to lower respiratory tract causing complications like pneumonia. The choice of anti-viral for management of RSV and influenza virus infection is ribavirin and oseltamivir, respectively. Thus, RSV, Human influenza virus and SARS-CoV-2 have similar clinical presentation, which needs to be distinguished to institute infection control measures and initiate appropriate therapeutic interventions.

In this pilot study we assessed the prevalence of RSV, Influenza virus and SARS-CoV-2 infection in patients presenting with SARI to tertiary care hospital. The prevalence of RSV in our study was 22% which agrees with other studies [16,17]. In a large study conducted in United States, Bin Lu et al. indicated higher prevalence of RSV B as compared to RSV A in elderly individuals [18]. This corroborates in our study as well, as mean age of our study population was 37 years. Geographic and seasonal variation in infections due to RSV A and B strains is common. In Indian setting, the prevalence of RSV infection in children varies from 5% to 54%. A prior Indian study from Eastern

Table 1: Demographic data of the 100 study participants from western Maharashtra, India with acute respiratory infection.

Characteristics of participants	Total, n=100
Gender, Male	65
Patient Age, Median (years)	37
Inter quartile range	25.75–52.00
Location (Districts of Maharashtra state, India)	Total, n=100
Nashik	70
Pune	30
Clinical features	
Fever, Cough and breathlessness	81
Fever with cough	63
Fever with breathlessness	27
Other signs/symptoms (wheeze, hemoptysis, vomiting, diarrhea, SpO2 <90%)	30
Abnormal chest X-ray	36

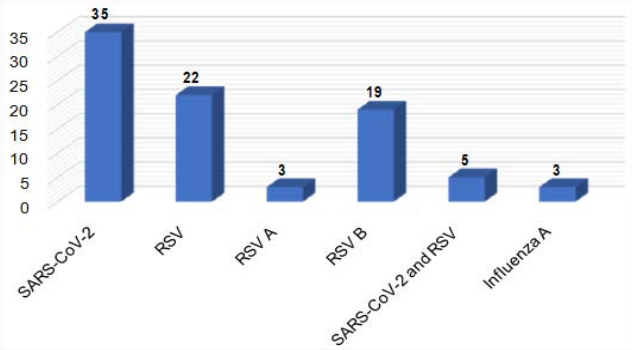

Figure 1: SARS Coronavirus-2, Human Influenza virus A and Respiratory syncytial virus A & B positivity by RT-PCR in 100 nasopharyngeal samples from study subjects in western Maharashtra, India with SARI.

India, reported significantly higher detection rate of RSV B as compared to RSV A [20]. Also Arankalle et al. reported IgG anti-RSV seroprevalence of 80% in western India, indicating high exposure to RSV in Indian adults [21]. There is scanty data from India on RSV co-infection in individuals with SARS-CoV-2 infection. Indian study conducted during early phase of COVID-19 pandemic among travelers returned back from foreign travel showed co-infection in 2.7% [22]. We observed RSV and SARS-CoV-2 co-infection in 5% of individuals with SARI. Also 17% of symptomatic patient's without SARS-CoV-2 infection showed presence of RSV infection which indicates need for screening other common respiratory viruses during current COVID-19 pandemic.

The prevalence of human influenza virus in this study was 3% with presence of pandemic 2009 H1N1 type only. No co-infection with SARS-CoV-2 was observed in this study. Integrated Disease Surveillance Program in India reported 114,667 cases of H1N1 between 2010 and 2017 with state of Maharashtra accounting for 21% of cases [23]. The decreasing trend of H1N1 during current pandemic is noteworthy.

The clinical presentation of RSV and Influenza virus infection in our study, including the predominance of fever, cough and breathlessness closely resembles that of COVID-19. We did not observe any difference in disease severity in mono-infected or co-infected individuals. As seen in polio, by virtue of interference, during co-infection, a virus may competitively inhibit replication of other. Whereas, during bacterial co-infection, increased severity of COVID-19 illness is noted. Although the study is limited by sample size, we used a sensitive molecular tool, real time PCR to detect infection. Other limitation of this study includes lack of follow-up data of the individuals with co-infections, as the samples were referred to us from different hospitals. Also, we could not assess other viral and bacterial co-infection due to resource constraints.

Conclusion

RSV infection in adults cannot be underestimated in current scenario. Human influenza virus infection is low in present setting of COVID-19 pandemic. Early diagnosis and instituting infection control measures are important to limit the spread of respiratory viral infections.

References

1. Stockman LJ, Curns AT, Anderson LJ, Fischer-Langley G. Respiratory syncytial virus-associated hospitalizations among infants and young children in the United States, 1997–2006. Pediatr Infect Dis J. 2012;31(1):5-9.
2. Falsey AR, Walsh EE. Respiratory syncytial virus infection in adults. Clin Microbiol Rev. 2000;13(3):371-84.
3. Collins PL, Melero JA. Progress in understanding and controlling respiratory syncytial virus: Still crazy after all these years. Virus Res. 2011;162(1-2):80-99.
4. Griffiths C, Drews SJ, Marchant DJ. Respiratory syncytial virus: infection, detection, and new options for prevention and treatment. Clin Microbiol Rev. 2017;30(1):277-319.
5. Fukuyama S, Kawaoka Y. The pathogenesis of influenza virus infections: The contributions of virus and host factors. Curre Curr Opin Immunol. 2011;23(4):481-6.
6. Krishnamoorthy S, Swain B, Verma RS, Gunthe SS. SARS-CoV, MERS-CoV, and 2019-nCoV viruses: An overview of origin, evolution, and genetic variations. Virusdisease. 2020;31(4):1-13.
7. Sulaiman KM, Muhammad T , Rishad Muhammad AP, Afsal K. Trace, quarantine, test, isolate and treat: A kerala model of COVID-19 response. medRxiv. 2020.
8. QIAamp® Viral RNA Mini Handbook for purification of viral RNA from plasma, serum, cell-free body fluids, and culture supernatants. 2020.
9. van Elden LJR, van Loon AM , van der Beek A, Hendriksen KAW, Hoepelman AIM, van Kraaij AIM, et al. Applicability of a real-time quantitative PCR assay for diagnosis of respiratory syncytial virus infection in immunocompromised adults. J Clin Microbiol. 2003;41(9):4378-81.
10. Detection of respiratory viruses by one step real time RT PCR.
11. National Institute of Virology, Indian council for Medical research. SOP for First Line Screening Assay for 2019. 2020.
12. National Institute of Virology, Indian council for Medical research. SOP for Confirmatory Assay for 2019-nCoV. 2020.
13. World Health Organization, Geneva. COVID-19 India situation report -27.
14. Garcia-Vidal C, Sanjuan G, Moreno-García E, Puerta-Alcalde P, Garcia-Pouton N, Chumbita M, et al. Incidence of co-infections and super infections in hospitalised patients with COVID-19: A retrospective cohort study. Clin Microbiol Infect. 2021;27(1):83-8.
15. Brandenburg AH, Neijens HJ, Osterhaus ADME. Pathogenesis of RSV lower respiratory tract infection: Implications for vaccine development. Vaccine. 2001;19(20-22):2769-82.
16. Hindupur A, Menon T, Dhandapani P. Epidemiology of respiratory syncytial virus infections in Chennai, south India. Clin Epidemiol Global Health. 2019;7(3):288-92.
17. Kini S, Kalal BS, Chandy S, Shamsundar R, Shet A. Prevalence of respiratory syncytial virus infection among children hospitalized with acute lower respiratory tract infections in Southern India. World J Clin Pediatr. 2019;8(2):33-42.
18. Bin Lu, Liu H, Tabor DE, Tovchigrechko A, Qi Y, Ruzin A, et al. Emergence of new antigenic epitopes in the glycoproteins of human respiratory syncytial virus collected from a US surveillance study, 2015–17. Sci Rep. 2019;9(1):3898.
19. Broor S, Parveen S, Maheshwari M. Respiratory syncytial virus infections in India: Epidemiology and need for vaccine. Indian J Med Microbiol. 2018;36(4):458-64.
20. Agrawal AS, Sarkar M, Ghosh S, Chawla-Sarkar M, Chakraborty N, Basak M, et al. Prevalence of respiratory syncytial virus group B genotype BA-IV strains among children with acute respiratory tract infection in Kolkata, Eastern India. J Clin Virol. 2009;45(4):358-61.
21. Arankalle VA, Kulkarni R, Malshe N, Palkar S, Lalwani S, Mishra AC. Seroepidemiology of respiratory syncytial virus in western India with special reference to appropriate age for infant vaccination. J Med Virol. 2019;91(8):1566-70.
22. Potdar V, Choudhary ML, Bhardwaj S, Ghuge R, Sugunan AP, Gurav Y, et al. Respiratory virus detection among the overseas returnees during the early phase of COVID-19 pandemic in India. Indian J Med Res. 2020;151(5):486-9.
23. Chatterjee P, Seth B, Biswas T. Hotspots of H1N1 influenza in India: Analysis of reported cases and deaths (2010-2017). Trop Doct. 2020;50(2):166-9.