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Review Article

Respiratory Syncytial Virus in During COVID-19 Pandemic: The Calm before the Storm or a Real Decline in RSV Positive Cases?

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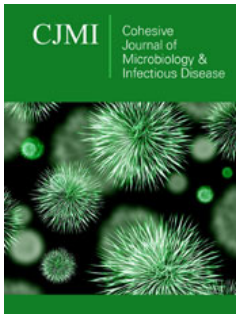
ISSN: 2578-0190



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Submission: October 26, 2022
Published: December 05, 2022

Volume 6 - Issue 2

How to cite this article: Moslem Ghaseminia. Respiratory Syncytial Virus in During COVID-19 Pandemic: The Calm before the Storm or a Real Decline in RSV Positive Cases?. Cohesive J Microbiol Infect Dis. 6(2). CJMI. 000635. 2022.
DOI: 10.31031/CJMI.2022.06.000635

Abstract

Respiratory Syncytial Virus (RSV) dispatches millions of children and high-risk adults to the hospital every year. In many cases, RSV leads to the death of patients. Some circumstances in the world influence the rise and fall of RSV. Among these cases, respiratory disease pandemics such as the H1N1pdm09 and COVID-19 can be mentioned. According to previous studies in 2009, the H1N1 influenza pandemic has changed the circulation pattern of respiratory viruses for several years, especially RSV. One of the explanations for these changes in the circulation of other respiratory viruses can be some approaches such as closing schools and observing social distancing to overcome epidemics. In this study, using past data and newly published studies, this change of patterns has been investigated in influenza and covid-19 pandemics. Based on previous studies, we have found that measures such as social distancing and school closures have also affected the type of RSV circulation in the Covid-19 pandemic. However, positive cases continue to spread despite the changes in the frequency of RSV, and the possibility of RSV epidemics in the coming years is not far from expected.

Keywords: Respiratory syncytial virus; SARS-CoV-2; Influenza; COVID-19; Pandemic

Abbreviations: RSV: Respiratory Syncytial Virus; COVID-19: Coronavirus Disease 2019; H1N1pdm09 Virus: 2009 H1N1 Pandemic; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; N Protein: Nucleoprotein; L Protein: Large Protein; P Protein: Phosphoprotein; CHD: Congenital Heart Disease; MPO: Myeloperoxidase; NE: Neutrophil Elastase; UK: United Kingdom; CDC: Disease Control and Prevention; TDH: Tennessee Department of Health; PIV: Parainfluenza Viruses

Introduction

Respiratory Syncytial Virus (RSV) hospitalizes nearly 3.2 million children under the age of five each year and causes hundreds of deaths in children, especially in low- and even middle-income countries [1]. In addition to children, young people are not safe from this virus. RSV is of particular importance in all age groups due to re-infection during life [2]. RSV is considered a significant threat in people over 5 years of age, especially in immunocompromised and elderly people. In these individuals, RSV increases the risk of severe respiratory infection and hospitalization in intensive care units, and even the mortality rate [3]. However, RSV is one of the most important problems in the health of infants. It has been shown that most infants will get RSV infection early in their life. Previous studies have shown that nearly 20% of infants in the first year of life exist wheezing caused by RSV, of which 2%-3% lead to hospitalization and require special care. For example, based on published studies, it is estimated that more than 100,000 infants in the United States are hospitalized due to RSV infection each year, and approximately 200 die from RSV infection each year [4,5]. Studies have shown that RSV can maintain its ability to reproduce for nearly 6 hours outside the host's body in the external environment, which makes RSV one of the most contagious viruses. This feature of RSV can cause contamination among children in schools and kindergartens [6]. Wheezing and hypoxia in neonatal bronchiolitis are distinct clinical features of RSV in this group of patients and lead to the high number of hospitalizations of infants with these symptoms in the United States [7].

Based on previous studies, we know that RSV outbreaks in certain months and seasons, especially in winter. Some circumstances in the world and especially in some countries affect this trend of increase and decrease of RSV. Epidemics, especially respiratory epidemics, are among these. Data from 2009 H1N1 Pandemic (H1N1pdm09 virus) show that it is also unclear how long it will take for a typical winter RSV season to resume in Australia and globally. The H1N1pdm09 virus has had an impact on the way respiratory viruses circulate for several years [8]. The response to these epidemics logically creates changes in human behavior, especially in society. Closing schools, kindergartens, and universities turning to work, observing social distancing, presence of people in gatherings with face masks, closing borders and restrictions on inter-city and inter-country travel, and finally welcoming strict health measures in Comparison with normal conditions compared to the time of the pandemic can be one of the main reasons for this change in the circulation of viruses in society [9]. Because respiratory viruses all have closely related and similar transmission routes, these massive and community-wide measures to deal with dominant infections in pandemics such as the influenza pandemic and the COVID-19 pandemic inadvertently affect the epidemiology of other respiratory viruses such as RSV has a direct effect [10].

Although the hypothesis of a lower prevalence of other respiratory viruses, such as RSV, under the exceptional circumstances of social distancing in the COVID-19 pandemic seems reasonable, it needs to be explored with more perspective on why and how this is the case. By studying past studies, questions ask: Is the reduction in RSV prevalence during the COVID-19 pandemic specific to the present or does it have a real impact on the spread of this virus in the future? Does RSV change in frequency at different ages? Do adults also get RSV infections, and do they have a role in the circulation model of this virus? The aim of this review is to understand the circulation pattern of RSV in populations during the pandemic and after the pandemic.

RSV structure

RSV has a negative-stranded linear RNA genome with a size of about 15kb that codes for 11 proteins (10 genes) [11]. The surface proteins of protein G (attached glycoprotein) and F (fusion) are among the main viral antigens in causing disease and play a major role in the pathogenesis of RSV. The binding of RSV to the cell is done by the G protein and then the F protein causes the fusion of the plasma membrane of the virus with the plasma membrane of the host and in this way, it enters the target cell. The accumulation of multinucleated cells takes place through the fusion of the plasma membrane by protein F, which creates syncytia in the cell. The reason for naming the virus as respiratory syncytial virus is this function of the F protein. This phenomenon allows the transmission of the virus from cell to adjacent cell. Epidemiological studies have shown that RSV has 2 main antigenic subtypes, A and B, both of which have been observed in communities in seasonal outbreaks [6].

Nucleoprotein (N), Large protein (L) and Phosphoprotein (P) are three viral proteins essential for RSV genome replication. N, by binding to RNA, causes the formation of a tightly woven helical complex and protects the RNA from recognition by the innate immune system and cellular nucleases. L, having enzymatic domains with RNA-dependent RNA polymerase (Rdrp) activities, methyltransferase domain for cap methylation and transcription of viral genes, and polyribonucleotidyltransferase domain plays an important role in viral genome replication. Finally, P, in addition to preventing the connection and association of nascent N (N0) with the RNAs of the host cell, with the property of polymerase cofactor, causes the binding of the viral L protein (Rdrp) to the nucleoprotein-RNA complex [12]. Each of these surface proteins (F and G) and proteins related to genome replication (N, L, and P) are suitable targets for drug and vaccine design [13,14].

Prevention and treatment for RSV

Due to the lack of access to effective treatments for RSV in children, prevention of RSV disease outbreaks is widely considered to be the most appropriate strategy. So far, various vaccines with different platforms have been studied and evaluated for RSV, but currently no approved vaccine is available for children and other age groups [15]. Nevertheless, palivizumab monoclonal antibodies are the only FDA-approved options available for only a small subset of infants younger than 2 years of age with Congenital Heart Disease (CHD), chronic lung disease [16]. Nirsevimab is another product that has been investigated as a long-acting mAb to prevent RSV in infants. Some studies have estimated the efficacy of nirsevimab in term and preterm infants to be 79.5% in phase 3 studies [17,18]. Also, studies have been conducted with the aim of comparing mutavizumab with palivizumab, both of which target the mentioned monoclonal antibodies of RSV glycoprotein F. Preliminary results show that motavizumab reduced the incidence of RSV-related hospitalizations in high-risk infants by 26% compared with palivizumab [19].

However, the results of this comparison should be considered for countries that have both widely available monoclonal antibodies and are able to choose surrogates, Because the smallest impact can have the biggest benefit in the future during the virus pandemic. Passive immunization of the mother is also one of the recommended methods to prevent the severity of RSV disease in infants. The use of this method to create immunity in infants against neonatal influenza and pertussis infection through the vertical transfer of IgG antibody has been recommended and carried out in many countries. Considering the limitations of using RSV monoclonal antibodies in newborns, RSV immunization of the mother and transfer of immunity to the newborn is an attractive preventive strategy in newborns that needs more detailed investigations [20]. As well as the presence of IgA antibody as the main antibody transferred through breast milk can also help the baby's immunity [21]. For the weak effect of this issue, studies should be conducted to show whether the small amount of IgA transferred through breast milk can have an effect in immunizing the baby against RSV as a

respiratory infection or not. In a study conducted by Hogan AB et al. [22] in 2017 in Australia, using a mathematical model, RSV vaccine mothers showed 30-46% in children aged 3-5 months and up to 37% in children under 3 months of hospitalization. By reducing RSV infection. Although more criteria should be taken into account to reach a final and reliable result, overall, this method shows that mother-fetal antibody transfer and immunity of newborns is not far from expected [22]. The lack of availability of an effective vaccine plays a very important role in the spread of viral infections, especially respiratory infections. Despite many efforts to achieve an effective vaccine against RSV, there is still no vaccine approved for all age groups to overcome RSV [23]. It seems that the vaccine has a more important role in reducing the frequency of respiratory viruses than other preventive measures.

Immune response to infection with RSV

Although in many cases RSV infection has a relatively mild clinical course and few cases of children end up being hospitalized, due to the high prevalence of this virus in children, especially infants during the first year of life (estimated to be 50%) and are hospitalized. Understanding the epidemiological and pathological mechanisms of RSV, especially in the lower respiratory tract, will clarify the approaches to deal with this disease. Airway edema due to excessive mucus secretion during extensive RSV inflammation, which is accompanied by increased neutrophils and inflammatory cytokine levels, has been reported in some studies. Remaining cellular debris and excess mucus cause blockage of bronchiole channels in severe cases, which ultimately facilitates the possibility of air trapping and lobar collapse. Perhaps this is the reason why complaints of shortness of breath, wheezing and cough are the most mentioned in RSV infections. The increase in severity of the disease due to lung involvement and bronchiolitis can be life-threatening and requires admission to the special care department for some patients, especially premature babies [24].

When the immune system encounters viruses, different cells of the immune system are involved and play a role in clearing the infection. However, some immune cells may act as a double-edged sword. In lung autopsy samples from fatal cases of RSV, many neutrophil cells have been seen. Neutrophils can play a prominent role in lung physiopathology through the production of pro-inflammatory cytokines and the release of cytotoxic molecules. Edema, excessive production of mucous secretions, and death and deposition of epithelial cells in the airways can be caused by pro-inflammatory cytokines and cytotoxic molecules [25,26]. It is difficult to conduct studies to confirm this issue due to the difficulties in sampling from young infants, however, studies on laboratory animals can help. In the studies conducted on RSV-infected mouse models, it has been shown that neutrophil Myeloperoxidase (MPO), Neutrophil Elastase (NE), decreased airway mucin production, and decreased TNFα levels in the lungs of RSV-infected mice [27,28]. However, the limitations and shortcomings of RSV modeling in laboratory animals such as the poor replication of the virus in mice should also be considered. It is better to examine the clinical samples of infants with mild and severe disease to gain a clear understanding of neutrophil function in the pathogenesis of RSV bronchiolitis [26]. Based on antigenic and genetic analysis, RSV strains isolated from patients with respiratory symptoms are classified into two groups, A and B [29].

RSV in adults

Sometime after RSV was first identified in 1956, many reports of RSV infection in adults were published. It has been shown that reinfection may occur several times in a lifetime. In these reports, it was announced that adults with a history of cardio-pulmonary diseases and people with suppressed immunity are at risk of developing severe respiratory diseases caused by RSV [30]. RSV reinfection in adults is often mild, but it plays a role in circulation of virus in society. However, frail elderly people living in long-term care facilities or at home, severely immunocompromised individuals (ADIS patients), and adults with cardiopulmonary disease with severe respiratory illness from RSV reinfection seem to be at risk [31,32]. Annually, between 3 to 7% of healthy elderly people are infected with RSV, and in the winter season, about 10% of elderly people are hospitalized [33,34]. RSV infections in the elderly in the ambulatory setting evaluated in few studies. for example, in 2005, RSV was reported 9% in a prospective cohort study of healthy adults over 65 years of age in Rochester (New York). In another study conducted in the United Kingdom (UK), RSV was reported in 19% and 15% of adults aged 45-65 years and adults over 65 years of age with flu-like symptoms, respectively [35].

Based on the studies conducted, it can be stated that one of the common causes of acute respiratory disease in adults over 50 years old is RSV, however, due to the fact that the disease appears in a mild form in adults, the probability of hospitalization of these patients is less and the identification of patients It is delayed [36]. In the study by Fleming DM et al. [37] the burden of RSV in the UK was estimated and evaluated in the years 1995 to 2009 using multiple linear time-series regression. In this study, it is estimated that the possibility of hospitalization and death due to RSV in high-risk elderly people compared to low-risk people are 4 times and 2 times, respectively [37]. Primary infection and re-infection in adults are important because a mild infection can help spread the virus. In a study on the shedding of RSV during natural RSV infection in hospital personnel, who were mostly healthy and young adults, it showed that it lasted for an average of 3 to 6 days (in some patients up to 12 days), this issue shows the importance of the role of adults in spreading It shows the virus [38]. Studies conducted in order to understand the ways of transmission of RSV virus have shown that this virus is mainly spread by large respiratory droplets among people and in the environment outside the host's body (skin, gloves, and table) it is capable of infection for hours. to remain Therefore, it can be said that in addition to close person-to-person contact, surface contamination in adults' workplaces and in children's schools and kindergartens plays a role in the spread and epidemic of the virus [39,40]. According to the information we have from previous studies, adults (with an efficient immune system) are exposed to

re-infection with RSV, and mild clinical symptoms such as a cold are observed in these people [41]. These people should be affected by reports of transmission of the virus to other people and their role in causing RSV epidemics should be considered.

RSV in influenza pandemic

RSV and influenza viruses are the most important causes of death from respiratory infections [37]. Studies show that RSV caused 200,000-66,000 deaths in 2005 in children younger than 5 years [42]. Also, in 2008, 28,000 to 111,500 influenza-related deaths were reported in children under 5 years of age [43]. Due to the simultaneous circulation of influenza and RSV viruses, it is difficult to determine the burden of damage and mortality of each of these viruses. Also, it is difficult to differentiate these viral infections due to relatively similar clinical manifestations, and laboratory confirmation is required for each. Although there is a difference in the circulating virus load from year to year, many health centers do not have the possibility of laboratory confirmation of these viruses, each of these limitations makes it difficult to check the status of these viruses [44,45].

The 2009 pandemic highlighted the importance of implementing potential outbreak control methods with surveillance programs for respiratory viruses [46]. Despite the widespread and emergence of the H5N1 and H1N1pdm09 virus and causing high economic and human losses in societies, there have been positive consequences such as the adoption of surveillance programs for rapid detection of respiratory viruses in many countries involved in the pandemic [47]. Being aware of the viruses circulating in the society is very important and is very important in correct diagnosis and appropriate treatment and timely measures. In 2010, the Centers for Disease Control and Prevention (CDC) in collaboration with the Tennessee Department of Health (TDH) in the state of Tennessee, using a viral panel to detect respiratory viruses such as Influenza viruses, Enteroviruses, Metapneumoviruses, RSV, Parainfluenza viruses (PIV), and Adenovirus were designed and used [48]. In the special circumstances of creating a pandemic due to the spread of a respiratory virus and due to the adoption of some regulations to control the circulating virus and the cause of the pandemic, the possibility of other respiratory viruses being sidelined seems reasonable. This change in the prevalence of other viruses was clearly demonstrated in the 2009 influenza pandemic [8]. Landes [48] and colleagues reported interesting results in Tennessee states with the aim of investigating the prevalence of influenza and other respiratory viruses in different seasons from 2010 to 2012 according to the CDC protocol. They reported that RSV was the most common virus after influenza (the most common pandemic virus) and enteroviruses/rhinoviruses (the most common common cold).

Also, with extensive surveillance to identify other respiratory viruses, they reported that RSV and other respiratory viruses increased in the second season (2011 to 2012) compared to the first season (2010 to 2011) [48]. However, various factors can affect the prevalence of circulating influenza and RSV viruses, for example climatic and geographical differences. For example, in the study of Alonso WJ et al. [44], it was reported that in the tropical parts of Brazil, RSV was circulating more than influenza and was associated with mortality from respiratory infections in this region. These changes were more evident when the H1N1pdm09 virus was in circulation [44]. In another study conducted by Lovato Salas F et al. [49], it was reported that among the samples collected from hospitalized patients with respiratory problems in 2009 to 2010, influenza was more common in adults and RSV in children. Also, unlike the previously mentioned studies, no significant difference in their frequency has been observed in the first and second outbreaks of the epidemic. This study was conducted in the city of San Luis Potosí, one of the most populated cities in Mexico [49]. These studies show that, at least in the case of influenza pandemic, other factors such as geographical differences should be considered in predicting the spread of RSV during the pandemic and after the pandemic. Also, some other factors such as religious ceremonies such as the holy Hajj ceremony can affect these differences. In order to clarify the impact of pandemics such as the influenza pandemic on the changes in the prevalence of RSV, we must also consider such cases. For example, in a study published by Rashid et al. [50] in 2008, 37 of 205 British pilgrims with URTI symptoms (18%) were reported to be positive for RSV or influenza [50].

Such cases that have been spread in the recent years and before the 2009 influenza pandemic, probably can play a role in the spread of RSV in the influenza pandemic and should be considered in the corner of the mind for comparisons and judgments. In general, it can be understood that during the influenza epidemic, other respiratory viruses, including RSV, were associated with changes in their epidemiology and were affected by the influenza pandemic. However, after the end of the influenza pandemic, reports of RSV epidemic patterns are available. This shows the temporary effects of the pandemic on other respiratory viruses.

RSV infection during the COVID-19 pandemic

Since 2019, when the first case of SARS-CoV-2 was confirmed in Wuhan, China, more than 6 million deaths related to this virus have been reported [51]. Extensive measures of public health centers such as conducting a large number of tests, disinfection, contact tracing, physical distancing, etc. to an acceptable extent in addition to controlling SARS-CoV-2 and It affects the control of other respiratory viruses such as RSV and influenza [52].

Paul Stamm [9] and colleagues have investigated the prevalence of different types of influenza virus and RSV from 2018 to 2021 during the Covid-19 epidemic at the University Medical Center Mainz, Germany. In this study, it is reported that the positive cases of influenza type B and RSV decreased significantly compared to the years before the pandemic (2018-2019). In the study of Varela FH et al. [53], it was reported that despite the prevalence of 32.7% of SARS-CoV-2 in people with respiratory problems, RSV and influenza A and B were not detected in the group of people with case symptoms in the fall and winter of 2020 [53]. Many studies

recognize RSV as a seasonal virus, and the time of the epidemic and the duration of the virus circulation are largely related to the geographical situation [54].

Strict health measures were implemented to prevent the rapid spread of COVID-19, especially in the seasons related to respiratory infections, after the number of patients increased in all parts of the world. In different countries, various studies were conducted to understand simultaneous viral infections. For example, Nolen et al. [55] study reported a decrease in RSV burden in Alaska in 2019-2020 compared to previous years [55]. Despite there being studies and reports of RSV reduction, it should be considered that changes from year to year and even season to season have also been reported for RSV in the past, which makes it important to evaluate more studies on this matter [56].

Also, the difference in the behavior of the virus in different groups of patients, including high-risk individuals such as infants, children under five years of age, and adults, should be taken into account when deciding whether to decrease or increase the RSV burden. However, Saravanos et al. [57] have conducted a multicenter study in southeastern Australia. They report that the peak of RSV-related illness in 2020 has shifted from fall and winter to early summer compared to previous years. They also reported that the overall frequency of RSV infections increased in children aged 2 to 4 years. Although they have explained this increase in RSV infection in children aged 2 to 4 years due to an increase in referrals and tests, it should be noted that the virus is still circulating in the population and there is a possibility of an RSV epidemic in high-risk groups. The measures taken in the process of reducing the spread of the COVID-19 pandemic have had an impact on the frequency of RSV in some parts of the world. We have identified many cases of people of different ages infected with RSV during the corona pandemic in our laboratory (unpublished). However, due to the wide age range of patients and lack of availability of suitable treatment and vaccine for RSV, it seems that this decrease in frequency is temporary and will increase in the years after the pandemic.

Conclusion

RSV is known as one of the most common respiratory infections in infants, children under 5 years of age, and high-risk adults with the possibility of hospitalization and even death. RSV, like other respiratory infections, is affected by various global events. The spread of RSV during pandemics, especially influenza and covid-19 pandemics, is due to health issues and control laws to prevent pandemics. There are several reports of a reduction in the burden of RSV infection in different parts of the world. Despite these effects, as the influenza pandemic in 2009 was not the end of other respiratory infections, it is expected that the prevalence of RSV will rise as before after the subsidence of the COVID-19 outbreak. These conclusions indicate that the implementation of restrictions, at least in part, as was done during the COVID-19 pandemic, can help reduce the burden of RSV and other viral infections during epidemics. There is still a need to focus on the development of appropriate vaccines and treatments to control and treat RSV in different risk groups such as infants, children under 5 years of age, and adults.

References

1. Shi T, Denouel A, Tietjen AK, Campbell I, Moran E, et al. (2020) Global disease burden estimates of respiratory syncytial virus-associated acute respiratory infection in older adults in 2015: A systematic review and meta-analysis. J Infect Dis 222(Suppl 7): S577-S83.
2. Griffiths C, Drews SJ, Marchant DJ (2017) Respiratory syncytial virus: Infection, detection, and new options for prevention and treatment. Clin Microbiol Rev 30(1): 277-319.
3. Lee N, Lui G, Wong K, Li T, Tse E, et al. (2013) High morbidity and mortality in adults hospitalized for respiratory syncytial virus infections. Clin Infect Dis 57(8): 1069-1077.
4. Welliver RC (2003) Review of epidemiology and clinical risk factors for severe Respiratory Syncytial Virus (RSV) infection. J Pediatr 143(5): 112-117.
5. Boyce TG, Mellen BG, Mitchel EF, Wright PF, Griffin MR (2000) Rates of hospitalization for respiratory syncytial virus infection among children in medicaid. J Pediatr 137(6): 865-870.
6. Piedimonte G, Perez MK (2014) Respiratory syncytial virus infection and bronchiolitis. Pediatr Rev 35(12): 519-530.
7. Thompson WW, Shay DK, Weintraub E, Brammer L, Cox N, et al. (2003) Mortality associated with influenza and respiratory syncytial virus in the United States. JAMA 289(2): 179-186.
8. Mak GC, Wong AH, Ho WY, Lim W (2012) The impact of pandemic influenza A (H1N1) 2009 on the circulation of respiratory viruses 2009-2011. Influenza Other Respir viruses 6(3): 6-10.
9. Paula Lobo A, Cardoso-dos-Santos AC, Rocha MS, Pinheiro RS, Bremm JM, et al. (2020) COVID-19 epidemic in Brazil: Where are we at? Int J Infect Dis 97: 382-385.
10. Wasfi R, Steinmetz-Wood M, Kestens Y (2017) Place matters: A longitudinal analysis measuring the association between neighbourhood walkability and walking by age group and population center size in Canada. PLoS One 12(12): e0189472.
11. Afonso CL, Amarasinghe GK, Bányai K, Bào Y, Basler CF, et al. (2016) Taxonomy of the order *mononegaviruses*: Update 2016. Arch Virol 161(8): 2351-2360.
12. Gilman MS, Liu C, Fung A, Behera I, Jordan P, et al. (2019) Structure of the respiratory syncytial virus polymerase complex. Cell 179(1): 193-204.
13. Fearns R, Deval J (2016) New antiviral approaches for respiratory syncytial virus and other *mononegaviruses*: Inhibiting the RNA polymerase. Antiviral research 134: 63-76.
14. Cockerill GS, Good JA, Mathews N (2018) State of the art in respiratory syncytial virus drug discovery and development. J Med Chem 62(7): 3206-3227.
15. Gunatilaka A, Giles ML (2021) Maternal RSV vaccine development. Where to from here? Hum Vaccin Immunother 17(11): 4542-4548.
16. Øymar K, Skjerven HO, Mikalsen IB (2014) Acute bronchiolitis in infants, a review. Scand J Trauma Resusc Emerg Med 22(1): 23.
17. Domachowske JB, Khan AA, Esser MT, Jensen K, Takas T, et al. (2018) Safety, tolerability and pharmacokinetics of MEDI8897, an extended half-life single-dose respiratory syncytial virus prefusion F-targeting monoclonal antibody administered as a single dose to healthy preterm infants. Pediatr Infect Dis J 37(9): 886-892.
18. Hammitt LL, Dagan R, Yuan Y, Baca Cots M, Bosheva M, et al. (2022) Nirsevimab for prevention of RSV in healthy late-preterm and term infants. New England Journal of Medicine 386(9): 837-846.

19. Wu H, Pfarr DS, Johnson S, Brewah YA, Woods RM, et al. (2007) Development of motavizumab, an ultra-potent antibody for the prevention of respiratory syncytial virus infection in the upper and lower respiratory tract. J Mol Biol 368(3): 652-665.

20. Nunes MC, Madhi SA (2018) Influenza vaccination during pregnancy for prevention of influenza confirmed illness in the infants: A systematic review and meta-analysis. Human Vaccines & Immuno therapeutics 14(3): 758-766.

21. Mazur NI, Horsley NM, Englund JA, Nederend M, Magaret A, et al. (2019) Breast milk prefusion F immunoglobulin G as a correlate of protection against respiratory syncytial virus acute respiratory illness. The Journal of Infectious Diseases 219(1): 59-67.

22. Hogan AB, Campbell PT, Blyth CC, Lim FJ, Fathima P, et al. (2017) Potential impact of a maternal vaccine for RSV: A mathematical modelling study. Vaccine 35(45): 6172-6179.

23. Zheng Z (2022) Challenges in maximizing impacts of preventive strategies against Respiratory Syncytial Virus (RSV) disease in young children. The Yale Journal of Biology and Medicine 95(2): 293-300.

24. Carroll KN, Wu P, Gebretsadik T, Griffin MR, Dupont WD, et al. (2009) The severity-dependent relationship of infant bronchiolitis on the risk and morbidity of early childhood asthma. Journal of Allergy and Clinical Immunology 123(5): 1055-1061.

25. Johnson JE, Gonzales RA, Olson SJ, Wright PF, Graham BS (2007) The histopathology of fatal untreated human respiratory syncytial virus infection. Modern Pathology 20(1): 108-119.

26. Sebina I, Phipps S (2020) The contribution of neutrophils to the pathogenesis of RSV bronchiolitis. Viruses 12(8): 808.

27. Kirsebom F, Kausar F, Nuriev R, Makris S, Johansson C (2019) Neutrophil recruitment and activation are differentially dependent on MyD88/TRIF and MAVS signaling during RSV infection. Mucosal Immunology 12(5): 1244-1255.

28. Stokes KL, Currier MG, Sakamoto K, Lee S, Collins PL, et al. (2013) The respiratory syncytial virus fusion protein and neutrophils mediate the airway mucin response to pathogenic respiratory syncytial virus infection. Journal of Virology 87(18): 10070-10082.

29. Anderson LJ, Hierholzer JC, Tsou C, Hendry RM, Fernie BF, et al. (1985) Antigenic characterization of respiratory syncytial virus strains with monoclonal antibodies. Journal of Infectious Diseases 151(4): 626-633.

30. Falsey AR, Walsh EE (2000) Respiratory syncytial virus infection in adults. Clinical Microbiology Reviews 13(3): 371-84.

31. Englund JA, Sullivan CJ, Jordan MC, Dehner LP, Vercellotti GM, et al. (1988) Respiratory syncytial virus infection in immunocompromised adults. Annals of Internal Medicine 109(3): 203-208.

32. Falsey AR, Cann RM, Hall WJ, Criddle MM (1996) Evaluation of four methods for the diagnosis of respiratory syncytial virus infection in older adults. Journal of the American Geriatrics Society 44(1): 71-73.

33. Falsey AR, Hennessey PA, Formica MA, Cox C, Walsh EE (2005) Respiratory syncytial virus infection in elderly and high-risk adults. New England Journal of Medicine 352(17): 1749-1759.

34. Falsey AR, Cunningham CK, Barker WH, Kouides RW, Yuen JB, et al. (1995) Respiratory syncytial virus and influenza A infections in the hospitalized elderly. Journal of Infectious Diseases 172(2): 389-394.

35. Zambon M, Stockton J, Clewley J, Fleming D (2001) Contribution of influenza and respiratory syncytial virus to community cases of influenza-like illness: An observational study. The Lancet 358(9291): 1410-1416.

36. Sundaram ME, Meece JK, Sifakis F, Gasser RA, Belongia EA (2014) Medically attended respiratory syncytial virus infections in adults aged ≥50 years: Clinical characteristics and outcomes. Clinical Infectious Diseases 58(3): 342-349.

37. Fleming DM, Taylor RJ, Lustig RL, Schuck PC, Haguinet F, et al. (2015) Modelling estimates of the burden of Respiratory syncytial virus infection in adults and the elderly in the United Kingdom. BMC Infectious Diseases 15(1): 1-12.

38. Hall WJ, Hall CB, Speers DM (1978) Respiratory syncytial virus infection in adults: Clinical, virologic, and serial pulmonary function studies. Annals of Internal Medicine 88(2): 203-205.

39. Hall CB, Douglas RG (1981) Modes of transmission of respiratory syncytial virus. Journal of Pediatrics 99(1): 100-103.

40. Hall CB, Douglas RG, Geiman JM (1980) Possible transmission by fomites of respiratory syncytial virus. Journal of Infectious Diseases 141(1): 98-102.

41. Hall CB (2001) Respiratory syncytial virus and parainfluenza virus. New England Journal of Medicine 344(25): 1917-1928.

42. Shi T, McAllister DA, Brien KL, Simoes EA, Madhi SA, et al. (2017) 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. The Lancet 390(10098): 946-958.

43. Nair H, Brooks WA, Katz M, Roca A, Berkley JA, et al. (2011) Global burden of respiratory infections due to seasonal influenza in young children: A systematic review and meta-analysis. The Lancet 378(9807): 1917-1930.

44. Alonso WJ, Tamerius J, Freitas AR. (2020) Respiratory syncytial virus causes more hospitalizations and deaths in equatorial Brazil than influenza (including during the 2009 pandemic). An Acad Bras Cienc 92(1): e20180584.

45. Jansen AG, Sanders EA, Hoes AW, van Loon AM, Hak E (2007) Influenza-and respiratory syncytial virus-associated mortality and hospitalisations. European Respiratory Journal 30(6): 1158-1166.

46. Lawson AB, Kleinman K (2005) Spatial and syndromic surveillance for public health. John Wiley & Sons, USA.

47. Lombardo JS, Buckeridge DL (2012) Disease surveillance: A public health informatics approach. John Wiley & Sons, USA.

48. Landes MB, Neil RB, McCool SS, Mason BP, Woron AM, et al. (2013) The frequency and seasonality of influenza and other respiratory viruses in Tennessee: Two influenza seasons of surveillance data, 2010-2012. Influenza Other Respir Viruses 7(6): 1122-1127.

49. Lovato Salas F, Matienzo Serment L, Monjarás Ávila C, Godoy Lozano EE, Comas García A, et al. (2010) Pandemic influenza A (H1N1) 2009 and respiratory syncytial virus associated hospitalizations. Journal of Infection 61(5): 382-390.

50. Rashid H, Shafi S, Booy R, Bashir HE, Ali K, et al. (2008) Influenza and respiratory syncytial virus infections in British Hajj pilgrims. Emerging Health Threats Journal 1(1): e2.

51. World Health Organization (WHO) Coronavirus disease (COVID-19) dashboard.

52. Stamm P, Sagoschen I, Weise K, Plachter B, Münzel T, et al. (2021) Influenza and RSV incidence during COVID-19 pandemic-an observational study from in-hospital point-of-care testing. Medical Microbiology and Immunology 210(5-6): 277-282.

53. Varela FH, Scotta MC, Polese Bonatto M, Sartor ITS, Ferreira CF, et al. (2021) Absence of detection of RSV and influenza during the COVID-19 pandemic in a Brazilian cohort: Likely role of lower transmission in the community. Journal of Global Health 11: (05007).

54. Li Y, Reeves RM, Wang X, Bassat Q, Brooks WA, et al. (2019) Global patterns in monthly activity of influenza virus, respiratory syncytial virus, parainfluenza virus, and metapneumovirus: A systematic analysis. The Lancet Global Health 7(8): e1031-e1045.

55. Nolen LD, Seeman S, Bruden D, Klejka J, Desnoyers C, et al. (2021) Impact of social distancing and travel restrictions on non-coronavirus disease 2019 (non-COVID-19) respiratory hospital admissions in young children in rural Alaska. Clinical Infectious Diseases 72(12): 2196-2198.

56. Stensballe LG, Devasundaram JK, Simoes EA (2003) Respiratory syncytial virus epidemics: The ups and downs of a seasonal virus. The Pediatric Infectious Disease Journal 22(2 suppl): S21-S32.

57. Saravanos GL, Hu N, Homaira N, Muscatello DJ, Jaffe A, et al. (2022) RSV epidemiology in Australia before and during COVID-19. Pediatrics 149(2): e2021053537.