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# Review on Respiratory Syncytial Virus Infection among Older Adults and Transplant Recipients

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**Abstract**

**Children frequently contract respiratory syncytial virus (RSV), which is also more and more indicated as one of the significant respiratory pathogens in immunocompromised hosts and older adults. RSV could exacerbate underlying lung and heart conditions in elderly adults (1). Also, it might be linked to acute rejection as well as chronic lung allograft malfunction amongst lung transplant recipients (LTRs), along with considerable mortalities and morbidities in hematopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) recipients. There are currently few choices for treating severe RSV, and there is less information on how to manage RSV in older adults(2). RSV in older adults, SOT recipients, and HSCT recipients is thoroughly discussed in this study. Since nosocomial dissemination was documented, infection control and prevention techniques are essential to preventing epidemics. Developing monoclonal antibodies for immunoprophylaxis, antivirals, and vaccines is ongoing, although more study is still required in such crucial fields(3).**



## Introduction

The risks of a dangerous infection rising with age, RSV can be defined as one of the major causes of acute respiratory disease in older adults[4]. The virus cannot be distinguished easily from influenza depending only on clinical presentation, also it circulates with various winter respiratory viruses, majorly seasonal influenza. RSV is believed to be the second leading cause of fatalities and hospitalizations among US adults 65 and over, after only influenza in terms of medically severe respiratory tract diseases in adults [5]. RSV in adults has no known disease, and there is no approved vaccination for preventing it at this time. For protecting populations who are more likely to experience adverse RSV outcomes, such as older adults, several potential candidate vaccines are on the horizon. 10 RSV disease burden and epidemiology indicate that vaccines must be given

to infants under 6 months of age, children and infants between 6 and 24 months of age, pregnant women (to give newborns passive immunity), and adults 65 years of age and older[6]. The older adult population is the key topic of the presented paper[7]. For assessing the effect of novel treatment and prevention methods which will probably be made accessible in the US soon, it is crucial to identify and define the effects of RSV in older adults. Professionals in healthcare and public health must educate themselves on RSV to communicate the value of prevention to elderly patients and the general public[8].

## RSV Disease in Older Adults

Whereas the majority of infected adults experience minor diseases of the upper respiratory tract, RSV puts some hosts at risk of severe diseases[9]. Adult persons >65 years, people who have chronic pulmonary or cardiac diseases, and immunocompromised hosts, such as HSCT and SOT recipients, are at risk for developing severe RSV. Pneumonia and bronchiolitis are two lower respiratory tract diseases that are signs of a severe RSV infection. A medical condition like chronic obstructive pulmonary disease, asthma, or congestive heart failure could also become acutely worse as a result. Severe disease can result in higher oxygen needs, hospitalization, the requirement for ventilator assistance, and negative outcomes like death[10]. Boattini et al. discovered that approximately 29.5% of hospitalized older adults of age more than 65 years with lab-confirmed community-acquired RSV diagnosis also developed pneumonia throughout the winters of 2017–2018 and 2018–2019. New research indicated that patients who have underlying chronic kidney disease were more likely to develop pneumonia. The investigators also noted that patients who have obstructive sleep apnea or obese hypoventilation syndrome used noninvasive ventilation more frequently, similar to solid tumors, carried a mortality risk[11]. 10 The same time age saw research on hospitalized adults over 85 with nosocomial or community-acquired RSV, which found that the RSV or asthma has been linked to pneumonia in the study group; RSV, asthma, and influenza B also led to higher usage of NIV[12].

In both non-institutional and institutional settings, such as adult day care facilities, nursing homes long-term care facilities, and those who live at home, there are several reports on the incidence of RSV in older adults[13]. 12–28 In a comprehensive review, the rate estimates regarding the long-term care institutions were succinctly described and ranged from 1% to 13.5%. The genotyping related to all RSV-positive respiratory samples through a long-term care facility in Paris revealed nosocomial transmission of RSV in 2 neighboring wards. The arsenal regarding RSV diagnostics consists of reverse transcriptase-PCR viral culture, serology, fast antigen detection techniques, and molecular diagnostics. The last two are rarely applied in US clinical settings[14]. It is interesting that whereas RADT sensitivity ranges from 78 to 85% in pediatric patients, the test is much less sensitive in adults, with only a pooled sensitivity. Adults with prior RSV infections are thought to have developed immunity, which results in lower viral titers in the respiratory secretions and shorter viral shedding duration. Therefore, switching to molecular diagnostic methods in the case where the severe RSV disease in older adults seems sensible[15].

Clinical care for an elderly patient with severe RSV has been restricted to supportive care, such as hydration, rest, dietary support, fever control, and respiratory support through the use of ventilation (NIV/mechanical ventilation) or supplemental oxygen, if necessary[16]. Ribavirin is the only antiviral that has been approved and is currently being used in clinical settings for treating patients who are immune deficient. High-quality, large data are currently lacking to support using ribavirin in older patients with severe RSV. Palivizumab can be defined as one of the monoclonal antibodies that are licensed for prophylactic use in newborns and young kids who are at high risk of developing severe RSV[17]. It inhibits the action of F protein on the RSV envelope. 32 There are no clinical study results to date regarding the administration of palivizumab to older adults who have a severe case of RSV[18].

## RSV among Immunocompromised Adult Hosts

RSV recipients are the most often observed, according to earlier observational research. At the same time, recent data suggested a decreased rate[19]. In research that included 1,303 immuno-

compromised hosts who have respiratory disease, routine examination of the broncho-alveolar lavage fluid as well as multiplex PCR for 20 virus types were conducted. It has been shown that 35% of them had a viral infection[20]. With 8.2% of cases, RSV has been the 4th most widespread RVI among them. Despite the high transmission of nosocomial transmission—many outbreaks have been reported in transplant facilities—the infection is generally spread through respiratory droplets in the community[21]. Because RSV's clinical course tends to be more aggressive in the early post-transplant period in the case when such patients are getting the most intense immuno-suppressive treatments, the timing regarding transplantation is critical. Along with the seasonal epidemiology of RSV, this also exists[22].

**Clinical Manifestations**

RSV frequently results in a self-limited upper RTI in immunocompetent hosts, whereas SOT and HSCT recipients experience a protracted illness course due to weeks or months of extended viral shedding. In the case when put to comparison with other RVIs, pneumonia is related to higher mortality and morbidity in immunocompromised hosts and tends to proceed to more severe disease[23]. A bacterial co-infection was found in 15.1% of immunocompromised patients in ten-year retrospective cohort research, of whom 19.4% had bacterial pneumonia and 80.6% had bacteremia confirmed by BAL. Because RSV causes damage to the respiratory epithelium and increases bacterial adherence, bacterial co-infections enhance the likelihood of lower RTI progression. RSV-associated mortality rates are substantial, reaching 80%, and up to 50% of SOT or HSCT recipients with RSV advance to LRTI[24].

**Diagnosis**

Due to its enhanced specificity, sensitivity, and quicker turnaround time, nucleic acid testing is now a major diagnosis component. Multiple viruses can be concurrently tested using molecular methods and one sample. It is similarly crucial to take the sample's source into account. In immuno-compromised patients who have pneumonia, this virus might not be present in the nasopharyngeal specimens (NPSs), so a lower respiratory specimen is advised in cases of diagnostic ambiguity. Rapid antigen testing for RSV is possible, however it has poor sensitivity and little predictive value[25].

**Treatment**

Although diagnostic methods were greatly improved, well-proven and efficient RSV treatments are still difficult to find because there aren't enough placebo-controlled studies[26]. The sole FDA-authorized medication for treating a severe RSV infection is aerosolized ribavirin, a nucleoside with the action towards RSV that is exclusively allowed for use in young children and infants. Unfortunately, administering aerosolized formulation is time-consuming and costly. There are other intravenous and oral preparations, yet they have side effects including hemolytic anemia and leukopenia, and shouldn't be used when pregnant. Despite being the mainstay of care for RSV, ribavirin lacks conclusive proof of its effectiveness, which causes management to vary. Early research indicated that ribavirin and RSV intravenous immunoglobulin treatment together produced positive outcomes, especially when administered early in the respiratory illness course, yet the RSV IVIg was later voluntarily removed from markets following approval. Existing investigational medications are being developed that can potentially be useful in treating severe RSV, which will help fill the gap in the market[27].

**Prevention**

Even though several vaccine formulations are being developed, there’s currently no commercially licensed RSV vaccination. Palivizumab prophylaxis which has been approved for high-risk patients who are 2 years old or younger, is the only available form of prevention at this age. Concerning its off-label usage for the prophylaxis of RSV in the recipients of SOT and HSCT, there is no agreement. The cost for adults is high, and no studies were done to evaluate its use in SOT scenarios. Thus, it is essential to take infection control precautions to prevent RSV. In the case when RSV infection is initially suspected, wearing a mask, careful hand cleanliness, and establishing droplet and contact isolation are crucial measures[28].

**HSCT Recipients**

It is widely documented how common infection of RSV is in the adult recipients of the HSCT. In the earlier observational research, allogeneic HSCT recipients had a cumulative rate of 3.5%–9%, while those who had autologous HSCT had a cumulative rate of 0.4%–1.5%. 66,67 A rate of as high as 12% in patients with HSCT has been reported in more recent reviews employing modern molecular diagnostic assays. RSV is often a community-acquired illness in the general population, yet with the recipients of HSCT, nosocomial transmissions are often recorded and might account for 50% of cases. 47,68–71 Patients in the pre-engraftment phase or ⩽ 1 month after the transplant had greater risks of contracting RSV when compared to the engrafted patients throughout an RSV outbreak amongst the HSCT recipients[29]. Additionally, pneumonia and mortality complication rates are typically greater in pre-engraftment patients. Approximately two-thirds of patients experience progression to LRTI, which is frequently seen in patients who have undergone transplants of allogeneic stem cells, graft vs. host disease, mismatched donor transplants, myeloablative therapy, advanced age, and prolonged lymphopenia. About retrospective analysis of 181 recipients of the HSCT with the RSV, host, and transplant-associated variables seemed to have a greater impact on the probability of developing LRTI compared to viral variables. Conditioning with a high-dosage total body infection, smoking history, an absolute lymphocyte count, and the development of respiratory infections were all factors that were strongly linked to disease progression. ALC > 1000/mm3 seemed to act as a barrier to growth [17].

As it has been previously mentioned, immunocompromised patients frequently experience prolonged viral shedding. Prior allogeneic transplantation was substantially related to long-term viral shedding lasting longer than 30 days, which was particularly obvious in the patients who have RSV infection and median viral shedding duration. Regarding allogeneic recipients with URTI or LRTI and risk factors for the progressions to the LRTI, British guidelines advise inhaled ribavirin and IVIg. Palivizumab could be a secure choice for prophylaxis towards RSV amongst adult HSCT patients, even though it is not officially advised for preventing RSV infections in adults. An outbreak among adult patients was successfully stopped by active surveillance to detect RSV-infected patients, the implementation of required infection control measures, palivizumab prophylaxis for high-risk patients, and other measures. According to an assessment of treatment of the RSV in the adult recipients of the HSCT, the progression rate to the LRTI has been considerably lower in the patients who have received ribavirin than in those who did not, despite the type, length, or inclusion of an immunomodulator[20]. According to the same research, patients who received both aerosolized ribavirin and an immunomodulator treatment had somewhat better outcomes than those who received only aerosolized ribavirin alone[18].

## Thoracic

The adult SOT recipient population with lung transplants has been the subject of the most research, as they are more likely than other organ transplant recipients to have RSV-related mortality and morbidity. Without typical severe RSV signs, lung transplant patients might initially simply exhibit shortness of breath or mild alterations in pulmonary function tests. The RSV occurs around once in every adult lung transplant recipient, and approximately 40% of those patients go on to develop LRTI[11]. Even though the rate of mortality is lower in the LTRs when compared to the recipients morbidity is still high, and the rate of mortality is still substantial at 10%. One study found that graft dysfunction occurred in LTRs with RSV infections. LRTIs brought on by RSV were linked to long-term sequelae including BOS. These diminish the transplant patients' quality of life[22, 30].

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