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Respiratory Syncytial Virus: Transmission and Treatment

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ABSTRACT

Respiratory Syncytial Virus (RSV), a respiratory tract infection-causing virus with a global distribution and seasonal occurrence, is the second leading cause of death in children under one year old, after malaria. The Respiratory Syncytial virus is an enveloped negative-strand RNA virus from the Paramyxoviridae family primarily transmitted by droplets of a cough or sneeze. However, kisses between infected and healthy individuals can also rapidly spread the virus, especially among children. Typically, the virus causes symptoms such as coughing, sneezing, or a fever making it visibly like other infections or conditions. Young children may have apnea and overall be irritable. Confirmation of RSV diagnosis can be done through available RSV-card tests or through RT-PCR tests. Though there is no standard treatment for RSV infection, drugs such as Ribavirin and Synagis® (Palivizumab) are currently used for managing symptoms of RSV infection in areas that have access to such medications. Palivizumab is used to treat prophylaxis, the prevention of serious lower respiratory tract disease brought on by RSV in children at high risk of RSV disease, is the greatest preventative approach. Numerous clinical studies are being conducted right now to treat and prevent RSV infection. Most of the study focuses on children below the age of 5 years because they are the most vulnerable, but there is also research on the prevalence of RSV in older adults and the effects of maternal vaccination on infants through the antibodies made to fight against RSV infection. G protein, F protein, and SH protein are three crucial membrane proteins that make up the RSV structure. A vaccine containing both the F and G RSV proteins would offer more protection against RSV. The F and G protein stimulates antibody formation, which neutralizes the virus. The RSV treatment plans and vaccine trials within India, South Africa, the United States of America, and the United Kingdom show similarities and differences that could be utilized to develop a treatment plan for RSV. In the upcoming years, further research is required to produce a cheaper alternative that is accessible to all countries. This will help to establish a set, effective protocol for RSV to be used worldwide.

Keywords

Respiratory Syncytial Virus (RSV), Respiratory tract infection, Viral transmission, Viral treatment, Vaccine for RSV, Recent trends in RSV treatment.

Introduction

Respiratory Syncytial Virus (RSV), a respiratory act infection-causing virus with a global distribution and seasonal occurrence, is an enveloped negative-strand RNA virus from the *Paramyxoviridae* family primarily transmitted by droplets of a cough or sneeze, Annually there are various infections that contribute to pediatric deaths due to severe symptoms. These infections or conditions include Malaria, Pneumonia, and HIV. Among these diseases which are widely known and studied, Respiratory Syncytial Virus Infection, known as RSV, has caused 100,000 to 200,000 deaths of babies under the age of one every year [1]. Such statistics make RSV the second leading cause of death in children under one year old, after malaria. This has been an infection of concern for years but due to the complexity of the virus, there has been extensive research on treatments and vaccines, but none have been widely approved in a way that makes it accepted by many physicians and countries.

Despite the presence of RSV infections in previous years, there has been a significant rise in cases in the United States. News sources in the United States such as CNN have recently made note that "RSV case rates are high, even after an early surge this summer." The virus took a larger toll on pediatric hospitals as expected with previous records of RSV. As a country with more developed healthcare, not being able to control the spread properly or treat it due to a lack of treatment resources is a problem in less developed countries as well. This literature review aims to study and analyze how various countries are preventing and treating RSV, in order to make suggestions on what plans may be better for the countries that have heightened RSV cases [2].

Viral Structure and Transmission

Respiratory Syncytial Virus is classified as a pneumovirus due to its single-stranded, non-segmented, negative-sense RNA [3]. The notable structure of the respiratory syncytial virus includes three integral membrane proteins. These include a receptor attachment glycoprotein (G), a short hydrophobic (SH) protein, and a fusion protein (F). The G protein is required for virus attachment to a host cell, which is essential for the virality of the virus. The RSV can then multiply by producing phosphoproteins, nucleoproteins, and RNA-dependent RNA polymerase [4].

RSV is primarily transmitted by droplets, which form when an infected person coughs or sneezes and land on the eyes, nose, mouth, or another surface that is touched before contacting the face. Kissing is another frequent method of transmitting RSV from adult to child [4]. Most RSV patients are contagious for three to eight days, but others can transfer the virus without showing symptoms for up to four weeks [5]. The easy route of transmission puts multiple populations at risk of becoming infected. These include premature infants, young children with any birth defects of the heart or lungs, immunocompromised young children or adults, or older adults with any heart or lung disease. Premature babies are at risk because their lungs are not fully formed and are very fragile. Since they are fragile, they will damage quite easily [6]. They also do not have a very developed immune system. They do not have antibodies and other complex immune cells that would be helpful in fighting off bacteria, viruses, or fungi since they were born early. Typically, the mother's antibodies cross the placenta at higher levels during the third trimester but since the baby is not carried full term, the baby does not have strong immunity [7].

Detection and Diagnosis

Common symptoms of RSV infection include coughing, sneezing, wheezing, fever, and a runny nose. People also experience a loss in appetite, which is also common amongst other diseases. Typically, these symptoms show up at separate times when an individual is infected. Often young infants will display increased irritability, be lethargic, and have difficulty breathing with harsh coughing. RSV symptoms can last an average of three weeks.

RSV has similar yet some distinct symptoms in children. Children frequently exhibit apnea, which is a brief period of not breathing properly. The apnea is often observed through the strain of the chest or stomach or the flaring of the nostrils because of respiratory distress. Low oxygen levels may also be observed through the lips and fingertips turning blue [8]. Many children up to two years of age are then diagnosed with Bronchiolitis which is most distinguished by wheezing, which occurs when small airways in the lungs are infected and are very narrow. When the child breathes in and out, a high-pitched noise will be produced indicating that the child is having heightened difficulty breathing. The breathing issues are often preceded by fever and a runny nose but since these are also symptoms of the common cold, the wheezing allows the diagnosis [9].

RSV is usually diagnosed after testing confirms it. This can be accomplished using an antigen test or a molecular test. Antigen testing uses a nasal fluid sample to look for certain proteins. The Alere BinaxNOW® RSV card, for example, detects respiratory syncytial virus fusion protein antigen in nasal and nasopharyngeal specimens [10]. Such cards enable outcomes in as little as 15-20 minutes. This test is typically used in pediatric doctors' offices to diagnose RSV infections in children under five.

The genetic material of the RSV test in a nasal swab sample is analyzed in molecular tests. A reverse transcription-polymerase chain reaction (RT-PCR) test is available, like the Covid-tests most people have already done. These tests are typically performed on older children and adults who have less viral material in their nasal samples. The samples need to be sent to a lab, so it typically takes longer for these results to be released. Previously, RSV tests were not available at drug stores in the United States, so it was difficult for some families to determine what condition they have without going to a doctor's office. However, recently on May 16th, 2022, the U.S (United States). Food and Drug Administration authorized a non-prescription Seasonal Respiratory Virus RT-PCR-DTC test that can be purchased online or in-store. This test checks for influenza-A, influenza-B, RSV, and COVID-19. The test involves self-collecting a nasal swab at home, which is then sent to LabCorp for testing without the need to consult a doctor. This test allows earlier self-isolation if the individual tests positive for any four of the viruses [11].

Prevention

Attempts at prevention are just as important as treatments. Prevention in this case will prevent primary and secondary infections, which would then prevent lengthy hospital bills. Since RSV is a viral disease, following certain protocols can help prevent the spread of the virus carried through droplets. The best way to prevent the spread is by following the basic hygienic rules such as covering your mouth when coughing or sneezing, washing hands with soap and water, avoiding proximity, and sharing utensils when sick. These steps can help prevent the spread of many diseases from the common cold to more serious conditions like RSV. The COVID pandemic has demonstrated the importance of following these steps. It is also especially important to follow these protocols when with immunocompromised children and adults, when sick because they usually experience symptoms to a worse degree. Many of them experience heightened versions of these symptoms,

which often lead to other conditions that require more intense treatment [12].

The steps listed above are common everyday measures everyone should take to avoid the spread of the disease. Researchers are currently working on the development of vaccines to prevent the onset of RSV. Now, the best preventative measure is a drug called palivizumab, more commonly known by its brand name Synagis®. This vaccine is for infants and children who are susceptible to severe diseases, for example, children with congenital heart disease. Although this vaccine is a good preventative measure, it is not commonly used for those already suffering from RSV [13].

Treatments

Unfortunately, there is no set treatment for targeting the RSV infection itself. There are various medications and treatments that have been proven to lessen severe symptoms. These medications and treatments are usually readily available in the United States but there can be issues in availability in other countries.

As previously mentioned, RSV can induce fever and has a direct impact on respiratory system functions; therefore, infected individuals should drink plenty of fluids. Fluid intake can assist restore fluids lost due to fever or respiratory tract evaporation. Since the viral infection produces decreased appetite, patients may feel no need to consume fluids, thus extra fluids, or electrolytes, provided either orally or through an intravenous line (IV), might be advantageous for the recovery of patient. Increased hydration also reduces mucus viscosity, which could otherwise lead to congestion and trouble breathing. To improve oxygen levels, oxygen therapies such as nasal prongs, oxygen tents, or masks can be used. Bronchodilator drugs, such as albuterol, may also be delivered through nebulizer or inhaler.

Antivirals for RSV infection are usually only given to children after they have developed severe symptoms that have been prominent for more than a week or so. Currently, there are only two RSV antiviral drugs that have been approved by the FDA (Food and Drug Administration) and these are typically only used to prevent any further respiratory tract infections that develop after being infected with RSV. These drugs include Ribavirin and Synagis® [14]. Ribavirin is an aerosolized therapy meaning that the medication is made into small-diameter aerosol particles that can be inhaled. This therapy targets the lower respiratory tract and has been shown to inhibit RSV replication [15]. This therapy is often only used in children that have bronchiolitis [15]. Despite studies showing ribavirin administration in children decreased illness severity and oxygen therapy time, this medication must be given at the onset of the infection to be effective. High expenses, occupational exposure, and toxicity are some of the concerns about this drug.

The second approved medication known as Synagis® (Palivizumab) is used to treat Prophylaxis. The palivizumab or Synagis® packaging defines prophylaxis as "the prevention of serious lower respiratory tract disease caused by RSV in children at high risk of RSV disease." When the drug was initially approved by the FDA, a specific definition of "high risk" was not given so the American Academy of Pediatrics (AAP) have released statements on what conditions make a child have a higher risk of more severe symptoms [16]. This treatment may be beneficial to children 12 months or younger diagnosed with hemodynamically significant congenital heart disease (CHD). The population that would benefit more would be children with cyanotic heart disease, taking medication that controls congestive heart failure, and will later need cardiac surgery. It is also recommended for infants that deal with moderate to severe pulmonary hypertension, which would be a pulmonary artery pressure greater than 25 mmHg at rest of greater than or equal to 30 mmHg when exercising [17]. The main goal of the injection is to protect premature babies (being born at or before 35 weeks and are a maximum of 6 months of age) from any worsened respiratory issues since their lungs are extra vulnerable at that point in their life [18]. Motavizumab is another treatment that is considered a second-generation monoclonal antibody for RSV meaning that it is a combination of f receptor and antibody moieties. The drug is currently undergoing large-scale clinical studies, but it has been understood that motavizumab is stronger than palivizumab. If approved by the Food and Drug Administration, it would be a more effective for RSV treatment in infants and other high-risk groups. In one phase three trial it was found that in infants that received a maximum of 15/mg/kg/month injections during their first RSV season, there were 83% reduced RSV hospitalizations than when compared to those who received a placebo. It also seems to be promising as the immunogenicity, what immune responses it activates, and the pharmacokinetic profile, how the drug moves through the body, was like palivizumab which is already used [19].

RSV Vaccine Development

Though RSV infection has been prevalent in the United States for years, there has been no successful development of a safe and effective vaccine. RSV vaccine development started in the 1960s. The initial concept was to develop a formalin-inactivated RSV vaccine, but the product made had negative effects. It caused severe lung inflammation after the first natural infection in RSV-naive infants who were vaccinated. This vaccine-associated enhanced respiratory disease (ERD) raised concerns as it had caused two cases of death. Since then, extra research has been done regarding RSV and possible vaccination efforts especially since there still is not a set treatment plan that effectively targets the virus itself [20].

Doubts on the structure of the RSV protein itself made it difficult to finalize a working vaccine. Research conducted under the US (United States) National Institute of Allergy and Infectious Diseases found that a protein called the F protein, was used by the respiratory syncytial virus to fuse with cells and infect them. Once this was realized, the researchers were able to fix the protein in its perfusion form so that it could be utilized to stimulate antibody synthesis prior to the virus entering human cells. Though this was understood, the post-fusion form of the protein with major conformational shifts was not targeted by earlier vaccines. Similar to the development of the COVID vaccines, companies such as Pfizer and Janssen both have produced their own version of the

RSV vaccines. The vaccines from Pfizer and GSK both include the stabilized preF protein while the Janssen has a modified adenovirus that produces the preF protein and the pure protein in one vaccine. Moderna has also been working on a version of the vaccine that consists of modified mRNA that promotes the production of the preF protein once inside the cell.

As of December of 2021, it has been reported that there are four vaccine candidates alongside a monoclonal antibody treatment that are in late-stage clinical trials.

On August 25th of 2022, Pfizer announced the results of their Phase 3 trial in individuals 60 years or older. With 37,000 participants, Pfizer administered 120 micrograms of RSV preF or a placebo at a 1:1 ratio. When conducted it was found that the vaccine had an efficacy of 85.7% and was well tolerated with no reported safety concerns. These are very promising results and should mean that a vaccine will be available within the upcoming years in the United States and many other countries. After the distribution of the Pfizer-BioNTech COVID-19 vaccines to 181 countries which means that they have the means to distribute the vaccine to countries that have higher rates of RSV cases [21]. A similar trial is also being conducted for the Moderna mRNA vaccine in individuals 60 years of age or older [22].

Most trials that have been conducted were for intramuscular RSV vaccines in older adults. Alongside these trials, there have also been studies involving children from 6 to 24 months of age receiving an intranasal RSV vaccine. Just as with the other trials, there was the administration of the developed nasal spray and placebo, which started on June 3rd of 2021 with an estimated completion date in October 2023 [23]. In contrast to the vaccines being administered to children, research is being conducted so that the mother can be vaccinated for RSV prevention so that body will make antibodies that transfer across the placenta. This method has been tested during phase II trials of GSK and Pfizer vaccinations in 2021. The phase II trials conducted for Pfizer vaccines showed that the infants who were immunized had higher antibody titers. The vaccine proved to be 85% efficient in protecting babies against RSV infection. Pfizer stated that pregnant women immunized with the RSV vaccine protected their babies from developing the severe disease for 6 months, which is significant as infants that are 6 months or younger are at higher risk of severe disease [24].

In another study, researchers calculated the possible impact of maternal RSV vaccination on life-threatening RSV infection in babies. Due to an age-dependent decline in maternally acquired protective antibodies after birth, maternal immunization will only give transitory protection. Because transplacental antibody transfer is only effective after the third trimester of pregnancy, maternal vaccination may only provide minimal protection for premature infants. The model estimates that the percentage of cases prevented would be highest if the maternal vaccine were administered between 22-30 weeks (about 7 months) gestational age and that the percentage of cases prevented would begin to decrease after 30 weeks gestational age due to the time required to reach maternal antibody peak levels. Finally, researchers discovered that maternal vaccination at 30 weeks of pregnancy would prevent at least 62% of RSV-related PICU hospitalizations and 29-48% of RSV-related in-hospital fatalities, depending on vaccine effectiveness [25].

It is evident that many trials and further research is being conducted in many companies for RSV vaccines, but they all still have some way to go to be approved for administration. However, in November 2022, the European Commission approved the use of Beyfortus (Nirzevimab), a monoclonal antibody for RSV treatment. This injection was developed together by the pharmaceutical companies of Sanofi and AstraZeneca. This intramuscular injection was developed to prevent RSV lower respiratory tract illness in newborns and infants. Through a study of 1490 infants who were given either the RSV vaccine or a placebo, the vaccine was found to have an efficacy of 74.5% [26]. However, it is important to keep in mind that the study was funded by AstraZeneca and Sanofi so the study could have been conducted differently to yield promising results.

Where is RSV prevalent globally and what populations are at higher risk within those areas?

When looking from a global perspective, it has been found that RSV infections in children are prevalent in all countries, but only certain ones have done research on the rates of infection and how it has been treated.

India

One such country that has published research is India. Literature reviews have shown that the main populations of concern in India in the context of RSV infection in the <5 years age group with RSV detection rates of 2.1% to 62.4 % which is high compared to that of other age groups. Overall, it was also found that there were more cases among children from low-income and lower-middle-income countries [27].

When looking at the prevalence of RSV infection in children who were hospitalized because of respiratory tract infections in Southern India, over 90% of the children who were RSV-positive were under two years of age. When looking at research conducted amongst 383 children at St. John's Medical College Hospital at Bengaluru (Bangalore), Karnataka, India, it was found that 24.5% of the children tested positive for RSV and 5.5% had RSV and another respiratory virus such as adenovirus or some strain of influenza. Once it was determined that the child had multiple viral infections, various treatment methods including acetaminophen and increased liquid intake were used. These alternative treatments have been widely used due to Palivizumab, not being available in India and being nearly 50,000 Indian Rupees [28].

It was discovered that a high level of antibiotics, such as amoxicillin/amoxicillin-clavulanic acid/or ceftriaxone, were used. This is significant because antibiotics are only supposed to be given and administered for bacterial infections, as they do not work on viral infections. High doses of such medications for viral infections will have little to no effect on eradicating the virus.

Antibiotics used to treat viral infections can have more unwanted side effects such as rash, nausea, and diarrhea [29]. It can be assumed that the use of antibiotics for RSV treatment when there is no easily accessible treatment within India, could be the way that physicians meet parent demands. It could also be due to the lack of rapid testing for RSV like there is in the United States. India typically has separate labs from the hospital that conduct Immunochromatographic antigen tests to verify RSV infection. Since the infection is confirmed through an outside lab and there is a time delay in which the test is processed, it may cause the doctor to prescribe antibiotics in the meantime just to provide some sort of treatment.

Though the antibiotics could be beneficial if the child has developed a secondary bacterial infection even with RSV infection, it was determined that the use of antibiotics did not improve conditions in children younger than two years old as per a Cochrane or system review done on the effectiveness of antibiotics. Overall, the study revealed and strongly advised that hospitals perform routine diagnostics for respiratory pathogens to reduce the use of unnecessary antibiotics, as well as promote education on RSV infection prevention techniques among pediatric populations. Prevention strategies include covering coughs and sneezes, washing hands, and avoiding close contact. The same study found that there was a significance between exclusive breastfeeding in children over three months and a lower incidence of RSV-positive illness. Currently there is no set treatment for RSV in India, but it has been recommended by the AAP and the Ministry of Health and Family Welfare to use inhaled bronchodilators such as albuterol, corticosteroids, intravenous or oral fluids and/ or oxygen [27]. These are also used in the United States in more severe RSV cases.

South Africa

Another country with higher rates of RSV infection is South Africa. In South Africa, it has been estimated that 178,000-443,000 children under the age of five will be infected with RSV every year. According to Professor Cheryl Cohen, who heads the Center for Respiratory Diseases and Meningitis at the National Institute of Communicable Diseases, RSV is one of the most common causes of death in young children in South Africa [30]. Though there are risk factors for severe RSV infection around the world, there are a few that are more prevalent in South Africa. These risk factors include malnutrition, premature births, being younger than 6 months, vitamin A deficiency, environmental pollution, and pre-existing congenital heart disease [31].

Malnutrition is an important and prevalent risk factor in South Africa. Malnutrition in newborns is associated with the thinning or atrophy of muscle within the primary lymphoid organs, including bone marrow and the thymus. The location is of pertinence because these two organs produce B and T cells so the thinning or lack of nutrients will cause a decrease or inability of B and T cell production. It has also been noted that severe protein malnutrition can also cause thymus atrophy, which would reduce T cell production and activation.

The next risk factor that is prevalent is premature babies. One in seven babies in South Africa are born prematurely, as reported by Northwest University. Premature birth is defined as a baby being born three weeks before the estimated due date. This is believed to be because there is a lack of primary healthcare in rural areas so pregnant women often go to the hospital later in their pregnancy after complications have already started. Unfortunately, alcohol consumption, smoking and/or physical/emotional abuse are all prevalent in the country which cause premature births and birth defects [32].

Vitamin A deficiency was another factor that is a phenomenon seen in about 44.4% of preschool-age children in Africa overall [33]. Vitamin A deficiency has been known to reduce innate immunity by preventing the proper regeneration of mucosal barriers that may be destroyed by infections, which also affects the function of neutrophils, macrophages, and natural killed cells. Decreased function of neutrophils is a notable negative effect of Vitamin A deficiency in the context of RSV infection as the human body exhibits a strong neutrophil response to RSV infection [34]. Vitamin A is also important for the development of T-cells and B-cells. T-cells. Typically, T-cells are important in fighting secondary RSV infections.

When looking at studies conducted within South Africa, it is evident that there have been protocols for using palivizumab for children at risk of severe bronchiolitis [35]. There have also been RSV management guidelines that include supportive treatments for bronchiolitis including humidified oxygen, bronchodilators, corticosteroids, ribavirin, and montelukast. However, it has only been proven that inhaled bronchodilators and nebulized 3% saline have had benefits in treating RSV-related bronchiolitis [36]. South Africa does not seem to have any vaccines in trials but is waiting for the results of most of the trials that were previously described in this paper.

United Kingdom

The United Kingdom (UK) is another country with an elevated risk of RSV infection. RSV is projected to cause 40 million cases in children under the age of five each year, with 10% requiring hospitalization. RSV seasonality tends to coincide with the commencement of general practice (GP) visits for acute bronchitis in children, followed by the onset of acute bronchitis and hospital admissions due to respiratory disease in senior individuals 2-3 weeks later [37].

In the United Kingdom, these illnesses often occur between the months of October and March, with a six-week outbreak. RSV infection is often a minor and self-limiting sickness, but it can be severe enough to cause lower respiratory tract infection (LRTI) requiring hospitalization in neonates and infants, as well as substantial respiratory morbidities such as bronchiolitis, pneumonia, and even death. Every year, 2-3% of infants under the age of one are admitted to the hospital with RSV bronchiolitis [38]. Severe instances of RSV may necessitate hospitalization and, in certain cases, intensive care. There is currently no effective

treatment for RSV LRTI other than supportive care. Palivizumab is the only pharmacological prophylactic permitted in Europe for the prevention of major LRTI requiring hospitalization caused by RSV in children at considerable risk of RSV illness. Children at high risk of RSV hospitalization and chronic respiratory morbidity were assessed, including preterm infants (35 weeks (about 8 months) gestational age and under six months at the start of the RSV season), infants with CLD, and infants with hemodynamically significant CHD. This research demonstrates the cost-effectiveness of palivizumab versus no prophylaxis in babies at considerable risk of RSV hospitalization in the United Kingdom [38].

United States

When comparing research, it was noted that the United States has more statistics and findings related to viral infection due to its prevalence. Although the number of cases present does not surpass many other countries, the technology, and resources available allows the US to conduct more research. When looking at the research, as of February 2022, around 58,000 children under the age of 5 have been hospitalized due to RSV, and out of those 58,000 hospitalizations around 100 to 500 children died. These statistics are only directed toward children, when looking at older adults with RSV, there are around 177,000 hospitalizations. This is almost three times the number of hospitalizations among children. This may be attributed to the fact that most of the research conducted on RSV is usually targeted toward children [39]. As stated before, there is no set treatment plan for RSV, but there have been many attempts. Currently, there are antivirals such as Ribavirin and Synagis ® that are given to children. Most other treatment options deal with treating symptoms as they come, such as the administration of fluid for dehydration and/or attempts at improving oxygen levels through an oxygen mask. These treatment options are symptom specific. There have been attempts made by companies, like Pfizer and Janssen, to create a vaccine, but they are still in its testing stages. Overall, more research and testing are required before a proper treatment plan set for RSV patients is developed. As for risk factors within the United States, it is very much like that of the other countries discussed. Most of the patient population consists of infants, older adults, and other immunocompromised people. Since this virus targets the respiratory system, those with respiratory diseases are at serious risk.

Discussion

Though the approaches towards RSV of a few different countries have been discussed, the World Health Organization has made efforts for "Global Respiratory Syncytial Virus Surveillance". The original surveillance plan allowed for the tracking of RSV cases in 14 countries this plan spanned from November 2018 to October 2021 and focused on children younger than 2 years of age, severe diseases that required hospitalization, varying virus types, and full understanding of risk groups and disease burdens. e countries discussed previously within this paper are in the pilot phase, meaning it may take a few years for data to be published [40]. As of now, there is no set treatment protocol set for RSV. Most of the care given at hospitals is symptom-specific and usually works to reduce the symptoms that are a side effect of RSV. Standard treatment protocol for patients admitted for RSV includes fluid intake to restore any fluid lost due to fever and/or respiratory tract evaporation and oxygen therapies such as nasal prongs and oxygen masks to improve oxygen levels. Although these treatments are standard for most countries, there are some variances in their methods. For example, in India, the usage of high doses of antibiotics is common to treat RSV. The use of antibiotics for the treatment of viral infections are not common, but this may be because there are not many easily accessible treatments within India. South Africa, the United States, and the UK are more likely to utilize Synagis ® for high-risk patients, but many doctors in the UK are hesitant to use it due to its cost. Although there are some differences, the main objective of the treatment protocols used in each country is to reduce the symptoms that arise as a result of the condition. Further research is required to establish a set protocol.

Many studies have been conducted over the years in order to develop a reliable and safe RSV vaccine. A humanized immunoglobulin G-1 monoclonal antibody that binds to the RSV F-protein known as Palivizumab, is extremely potent in vitro against clinical RSV isolates of types A and B. The IMpact-RSV experiment was a randomized, double-blind, placebo-controlled trial that took undertaken at 139 different locations across the United States, the United Kingdom, and Canada. The researchers randomly assigned 1,502 preterm or bronchopulmonary dysplasia children to obtain five injections of palivizumab or a placebo every 30 days. After the trial, it was observed that palivizumab lowered hospitalization rates for RSV infection by 55% or more in children. These children also spent less time in the hospital and were admitted to the intensive care unit less frequently. Premature infants with no BPD experienced a 78% reduction in RSV hospitalization while children with BPD had a 39% reduction[41].A study conducted in the 1998-1999 RSV season in the United States of America and Canada with 56,000 infants showed that only 2.3% of the children that received palivizumab prophylaxis were hospitalized with respiratory tract infection, suggesting that the drug was effective. This suggests that the drug will become a standard treatment for RSV infection in the future if it can be produced for a cheaper price and distributed globally [28]. Despite significant research for RSV vaccines, researchers confront challenges in vaccine production because the danger of infection is greatest in very young infants, which means they would need immunization as soon as they are born when their immune systems are still maturing. The RSV F and G proteins, which trigger neutralizing antibody production, are glycoproteins that are weakly able to prove an immune response in early infancy. Furthermore, if the mother had previously been infected with RSV during her pregnancy, any maternal antibodies in the newborn would neutralize the RSV vaccine before the infant had the opportunity to establish an immune response. Natural immunity to any disease is transient and typically does not protect against the recurrence of infection, even in those with robust, mature immune systems. As a result, boosters would very certainly be required on a regular basis. A vaccine containing both the F and G RSV proteins would provide vast protection against RSV infections [42].

Future Trends

Although the course of RSV is highly unpredictable, further research will aid in establishing a set treatment protocol worldwide for the current treatment of the condition. The drug known as Synagis®, or by its generic name palivizumab, is commonly used in many countries for the prevention of RSV in high-risk patients. Out of all the countries discussed in this paper, the United States and South Africa are seen to have utilized Synagis® the most. In the UK and India, many practitioners are hesitant to use Synagis® because of its cost. With further research, more cost-efficient alternatives can be found to produce Synagis® at an affordable rate so that more countries are willing to utilize it. Other treatments such as Motavizumab are underway, but still, seek the approval of the FDA. Once it is approved, it can be used as an alternative treatment to Synagis®.

Though the research for this paper was done through October and November of 2022, RSV made news headlines more in November. Recently it has been reported that increased RSV infections are significantly burdening health systems in "Canada, Mexico, Brazil, Uruguay, and the United States" [43]. If these countries with more funding, accessibility to medications, and trials for vaccination development are struggling with the rise of RSV cases, it is difficult for other countries such as India and South Africa discussed above. More research would need to be done to determine what other countries may be doing to handle RSV cases.

Conclusion

It can be understood that the Respiratory Syncytial Virus has a threat to the health of a multitude of children across the world. Current developments for treatments and vaccines are very promising. The go-to treatments including Palivizumab and Ribavirin in countries that have ready access are promising and aid in getting children infected with RSV back to health. Further research is required for the development of a more cost-efficient treatment protocol accessible to all countries.

This paper is limited in that it only looks at treatments in the United States, and RSV infection situations in India, United Kingdom, and South Africa. As cases are increasing in the United States and other countries, it would be beneficial to keep track of cases and treatments used now and for the next few years to determine what treatment plans are more effective. Effective treatment plans can then be used as a basis and altered based on what medications are available in countries with high RSV cases as well, since vaccine importation may not be in effect right after vaccine approval.

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