

HUMAN RESPIRATORY SYNCYTIAL VIRUS

Abstract

Human Respiratory Syncytial Virus (RSV) has a significant role in the development of newborns' and children's respiratory tract illnesses. It causes serious lower respiratory tract infections in newborns and young children. RSV causes widespread outbreaks of illness each year during the winter season. In the winter months of November through March RSV outbreaks reach their peak in July, with 55-77% of cases primarily affecting children under the age of four. RSV can spread as cell-to-cell transmission also. The infection of RSV is localized only in the lung. The pathological findings of RSV infection are same as other respiratory infections. RSV is a primary viral infection, and treating it with antibiotics has no effect, But it can help the patients to escape from secondary bacterial infection. Currently, no medication is capable of completely curing RSV. As a result, taking preventative measures is preferable than treating individuals who have a high risk of complications.

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I. INTRODUCTION

Over the past few decades, the human respiratory syncytial virus has been recognised as a global disease of young infants. This virus has a significant role in the development of newborns' and children's' respiratory tract illnesses. The virus was initially discovered in a sick laboratory chimpanzee in 1956 during an outbreak that resembled the common cold.

Later, in 1957, Chanock and his coworkers isolated this virus from newborns suffering from lower respiratory illness. The Human Respiratory Syncytial Virus is the sole and most significant agent that causes serious lower respiratory tract infections in newborns and young children, according to all epidemiological research. The clinical signs of RSV infection can change depending on the patient's age. The main clinical symptoms of RSV infection in young infants and children include bronchitis and pneumonia. Older children and adults who repeatedly get sick with their upper respiratory tracts can spread the RSV to other people.

RSV causes widespread outbreaks of illness each year during the winter season. Mostly the infants are susceptible to this outbreak; increased susceptibility will be seen in following cases;

- Premature infants
- Infants with bronchopulmonary dysplasia
- Infants with chronic pulmonary diseases
- Infants with cardiac diseases
- Infants with immunosuppressed condition
- Institutionalized elderly adults

II. MORPHOLOGY

According to the electron microscopy model, the Human Respiratory Syncytial Virus has two distinct sizes and structures. One is an enveloped virus with a spherical shape and a diameter of 150–250 nm, and the other is a filamentous virus with a length of 10 μm. Single-stranded negative sense RNA serves as the genetic building block of this virus. Nucleocapsid encloses the viral genome. The entire virion is then encased in a lipid bilayer envelope that is contained within the virus. Hemagglutinin and neuramidase, two crucial proteins, are absent from this bilayer. Eight structural proteins and two significant glycoproteins, F- Fusion protein and G- Glycoprotein, are also present in this layer. The envelope included these two proteins as spikes of a glycoprotein.

The genome of the respiratory syncytial virus is single stranded negative sense RNA. The length of this RNA is roughly 15222 base pairs. About eight RSV proteins are encoded by the genome. The nucleocapsid's membrane shields the genetic material.

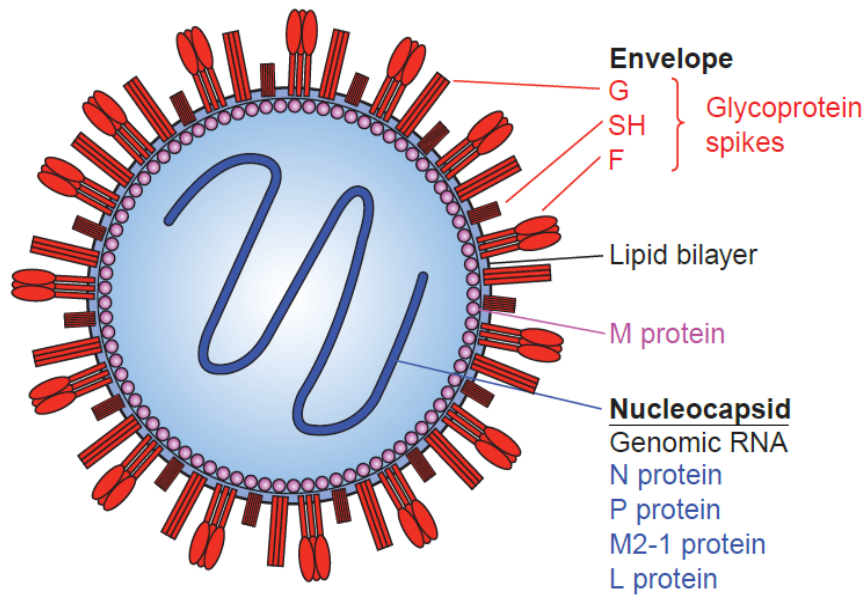


Figure1: Source- (<http://hdl.handle.net/10603/179392>)

III. CLASSIFICATION

The Paramyxoviridea family includes the human respiratory syncytial virus. The morphology, genomic structure, biological functions, and protein sequence relationships served as the basis for this classification. Once more, the paramyxoviridea family was divided into the pneumovirinea and penumovirus subfamilies. Human Respiratory Syncytial Virus was classified under the subfamily peumovirus.

IV. EPIDEMIOLOGY

Every year, the RSV outbreak will commence in the winter months of November through March RSV outbreaks reach their peak in July, with 55-77% of cases primarily affecting children under the age of four. Monophasic RSV epidemics were discovered in several places, and they also occurred annually.

RSV is the most frequent pathogen causing lower respiratory infections in newborns and accounts for one-fifth of all lower respiratory infections worldwide. RSV-related lower respiratory tract illnesses will be epidemic, and the epidemic may change with latitude, altitude, and climate.

The RSV outbreak will follow a seasonal pattern, typically based on altitude and regional variance. Epidemics will occur in groups over the winter months. Although these epidemics have a different appearance pattern from continent to continent, they typically start in coastal areas.

Table 1: Respiratory syncytial virus in hospital- based studies in India (1971- 2018)
Source : (<https://www.sciencedirect.com/science/article/pii/S025508572030579X>)

Place	Method	Setting	Cases	Age group	Number of studied	RSV positivity (%)
Vellore	Culture IFA	OPD/IPD	ARI	<6 years	809	10.7
Lucknow	Culture IFA	OPD/IPD	ARI	<5 years	736	5
Delhi	ELISA and IFA		ARI	<5 years	131	54-70
Delhi	IFA/ELISA	IPD	ARI		132	44
Delhi	CEC/IFA	IPD	ALRI	<5 years	200	17
Pune	IFT	OPD/IPD	ARI ALRI	<5 years	199 186	3.6 39.2
New Delhi	mPCR	OPD/IPD	ALRI	<5 years	301	20.2
Kolkatta	RT-PCR	OPD/IPD	ARI	<5 years	1091	8.7
Hyderabad	ELISA	OPD	Bronchiolitis, pneumonia	4-24 months	301	20.2
Bangalore	DFA	IPD	ALRI	<2 years	77	22.1
Pune	Multiplex RT-PCR	Sub-sample from laboratory	ILI/SARI	<5 years	843	15.4
Dibrugarh	RT-PCR	Sub-sample from laboratory	Routine flu surveillance	<6 years	493	7.95.4
Kolkatta	Real time RT-PCR	OPD/IPD	ILI/SARI	<12 years	764	916
Lucknow	RT-PCR	OPD/IPD	ALRI	<14 years	188	21.3
Chandigarh	Multiplex PCR	Community +	CAP/ALRI	<5 years	428	12.9
New Delhi	Real time RT-PCR	IPD	All cause admissions	<5 years	505	16.2
New Delhi	TAC real time RT-PCR	IPD	SARI	<5 years	425	35.1
Cuttack	RT-PCR	OPD/IPD	ARI ALRI	2-60 months	126	17
Bhubaneshwar	M-PCR	OPD	ARI	<12 years	332	4.2
Jabalpur MP	RT-PCR	OPD/IPD	ILI	<3 years	526	12
Lucknow	Real time RT-PCR	OPD/IPD	ILI/SARI	All ages	1653	12
Jaipur	Real time RT-PCR	OPD	ARI	<5 years	689	25.4

ARI: Acute respiratory infections, ALRI: Acute lower respiratory infection, RT-PCR: Reverse transcription-polymerase chain reaction, ILI: Influenza-like illness, CAP: Community-acquired pneumonia, SARI: Severe acute respiratory infection, RSV: Respiratory syncytial virus, CEC: Centrifugation-enhanced culture, IFA: Immunofluorescence assay, OPD: Outpatients department, IPD: In-patients department, DFA: Direct fluorescence assay, TAC: Taqman array card

V. PATHOGENESIS

The incubation period for RSV is nearly 4 to 5 days. The infection begins as upper respiratory tract infection. Entry of the virus is through contaminated droplet nuclei, then the viral particles are trapped by mucosal layer and infects the epithelial cells of nasopharynx. If the infection continues, it will be transferred to lower respiratory tract. The mechanism of transmission is unknown in this case. RSV can spread as cell-to-cell transmission also. The infection of RSV is localized only in the lung. Even in the severe cases also, there is no dissemination of viral particles in the blood and it never be systemic. With 3 day of the infection, the children may develop tachypnea which indicates the viral spreading to the lower respiratory tract.

The pathological findings of RSV infection are same as other respiratory infections. Epithelial cells will be destroyed during the infection and discharged as cell debris into the bronchiolar region. The mucosal secretions are also enhanced as a result. Following this, there will be a peri-bronchiolar inflammatory response, which results in infiltrates, particularly those containing mononuclear cells. Additionally, this causes edoema in the submucosal and mucosal layers. The combination of mucous secretions, submucosal edoema, and mucosal necrosis may cause bronchioli blockage. As a result, there occurs hyperinflation and atelectasis, which are the typical RSV symptoms.

VI. CLINICAL FEATURES

At the initial stage of the RSV infection the patients start with the symptoms of upper respiratory tract. rhinitis, cough and low-grade fever. If the infection proceeds for about two to five days, the RSV enters the lower respiratory tract and starts with the symptoms of lower respiratory tract. the symptoms of tachypnea, chest retractions and sometimes wheezing. During the infection at first time, many children will show the symptoms of lower respiratory tract and will be self- limited. But few children with predisposing factors may develop a severe infection and should be hospitalized for their treatment.

The RSV infection in the elder children and adult were presented with the common symptoms of mild upper respiratory tract infection.

VII. LABORATORY DIANOSIS

- 1. Sample:** Nasopharyngeal aspirate (NPA), nasopharyngeal wash (NPW), nasopharyngeal swab (NPS), oropharyngeal swab (OPS), nasal swab, nasal wash or a mix of specimens
- 2. Microscopy:** Electron microscope and Immunofluorescent microscopy can be used to demonstrate the presence of RSV in the clinical specimens.
- 3. Culture Method:** The Human embryonic kidney cell and Hep-2 cell culture method are the methods used for the culturing of Respiratory Syncytial Virus in the laboratories. The mink lung cells (Mv1Lu) and human adenocarcinoma A549 cells are also used in combination for the culturing of RSV as a commercial product.
- 4. Antigen Based Assay:** The methods of detecting the antigen from the clinical samples includes Immunofluorescent assay and immunochromatographic assay

- 5. Serological Method:** The detection of antibodies in the serum of infected patients can give the indirect evidence of RSV infection. Various antibodies will be produced against the RSV during the infection such as IgM, IgG and IgA antibodies. They can be detected by using ELISA method. A greater-than-fourfold rise in titer to any of the RSV antigens was considered diagnostic of recent infection. This method is highly sensitive and specific when compared to that of RADT but not as molecular method. The major disadvantage in this method is samples should be pooled and test as a batch. This also requires expertise and more time when compared to that of RADT.
- 6. Molecular Method:** Viral RNA was considered as the marker for RSV infection which can be detected by using the reverse transcriptase Polymerase Chain Reaction (rt-PCR). Several RSV genes have been used in various study includes SH, G and F gene. Among this F gene is coding for the fusion protein in Respiratory Syncytial Virus which consist of two regions F1 and F2. In this study, we have amplified F1 region of F gene, since it is common for both RSV A and RSV B group. This method is having a advantage of high sensitivity and specificity with fast diagnosis within few hours. But also having certain disadvantages includes risk of contamination and not available in many laboratories.

VIII. TREATMENT

The care of the clinical problems is part of the treatment. This can be accomplished by giving the kids bronchodilators to increase their respiratory activity. Patients may also be subjected to airway cleaning techniques including vibration and percussion. If a patient's oxygen saturation is below 90%, an oxygen supplement is required. RSV is a primary viral infection, and treating it with antibiotics has no effect, But it can help the patients to escape from secondary bacterial infection. RSV can be treated with the affordable antiviral medication ribavirin. However, studies show that giving ribavirin to RSV-infected patients produced problematic results.

Prophylaxis:

Currently, no medication is capable of completely curing RSV. As a result, taking preventative measures is preferable than treating individuals who have a high risk of complications. A humanized monoclonal antibody called Palvizumab that is directed against a particular RSV protein can be used as a preventative strategy. It can be administered intravenously or intramuscularly, and it will be effective against both the RSV A and B subunits. This will be especially useful for people with severe immunodeficiencies, cancer patients, and transplant recipients.

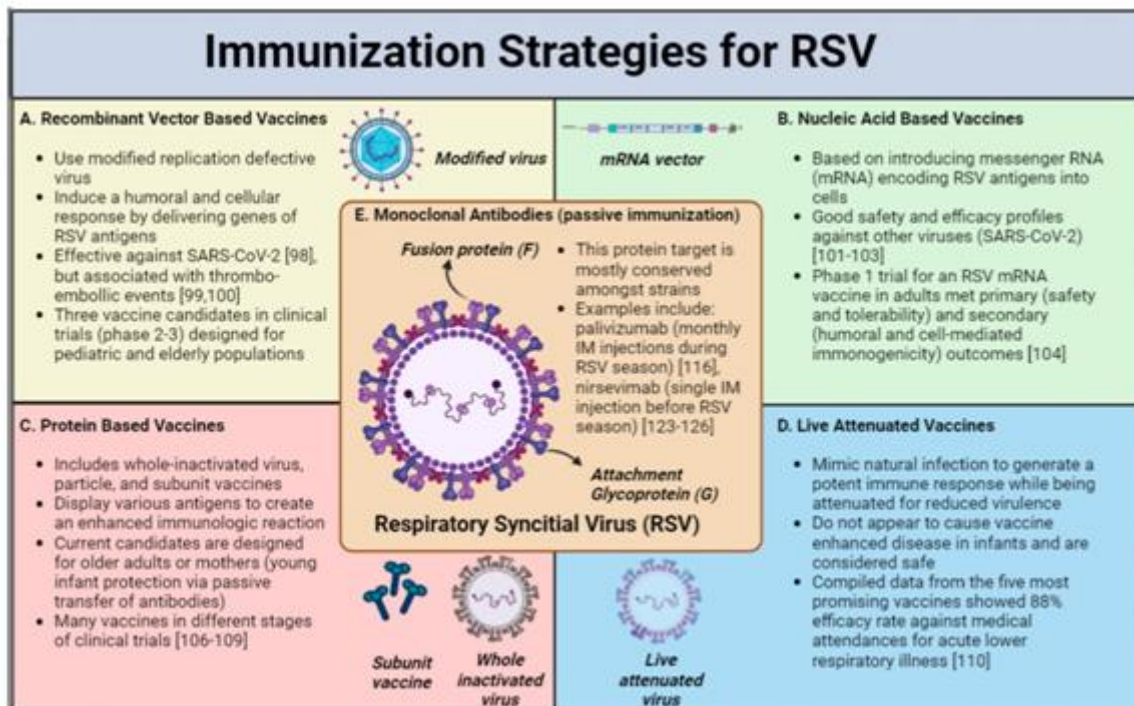


Figure 2: Source- Gatt D, Martin I, AlFouzani R, Moraes TJ. Prevention and Treatment Strategies for Respiratory Syncytial Virus (RSV). *Pathogens* [Internet] 2023;12(2):154. Available from: <http://dx.doi.org/10.3390/pathogens12020154>

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