

## Review Article

# Community transmission of a virus: a global pandemic overview

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### ABSTRACT

The word ‘pandemic’ was originally a derivative from two Greek words “pan” referring “all” and “demos” “people”. “An epidemic arising over a very diverse area, crossing the global margins, and typically affecting a huge number of people” is defined as a pandemic. Therefore pandemics are recognized by their topographical scale instead of severity of ailments. Even though the term “pandemic” has not been clearly defined, wide geographic extension, disease movement, novelty, severity, high attack rates and explosiveness, minimal population immunity, infectiousness and contagiousness can be considered as some of the key features of this term. Till today, globe has encountered several notable pandemics caused by virus such as Spanish flu, acquired immune deficiency syndrome (HIV/AIDS), smallpox, SARS, Ebola and Nipah disease whose causative organisms are H1N1, human immunodeficiency virus (HIV), Variola virus, DEN-1/DEN2/DEN3/DEN4, coronavirus, Ebola virus (Zaire/Sudan/Tai/Cote D’ivoire), and Nipah virus (NiV) respectively. This review includes detailed data regarding various viral pandemics. Analyzing the history, clinical manifestation, pathogenesis, management and precautions of several viral pandemics which will promote and spread the awareness among the public as well as the healthcare system.

**Keywords:** Community transmission, Corona virus, Influenza, Pandemic, Virus

### INTRODUCTION

Intermittent outbreaks of infectious diseases have had intense and lasting impact on the community throughout history.<sup>1</sup> The word ‘pandemic’ was originally a derivative from two Greek words “pan” referring “all” and “demos” “people”.<sup>2</sup> “An epidemic arising over a very diverse area, crossing the global margins, and typically affecting a huge number of people” is defined as a pandemic. Therefore pandemics are recognized by their topographical scale instead of severity of ailments.<sup>3</sup> Even though the term “pandemic” has not been clearly defined, wide geographic extension, disease movement, novelty, severity, high attack rates and explosiveness, minimal population immunity, infectiousness and contagiousness can be considered as some of the key features of this term. Most of all the crisis related to pandemic cause massive negative impact not only on the health and economy of various communities across the globe, but

also cause significant disruptions in security of social and political area.<sup>4</sup> It is estimated that nearly around 60% of all human infections are caused by one thousand different varieties of viruses.<sup>5</sup> Till today, globe has encountered several notable pandemics caused by virus such as Spanish flu, acquired immune deficiency syndrome (HIV/AIDS), smallpox, SARS, Ebola and Nipah disease whose causative organisms are H1N1, human immunodeficiency virus (HIV), variola virus, DEN-1/DEN2/DEN3/DEN4, coronavirus, Ebola virus (Zaire/Sudan/Tai/Cote D’ivoire), and Nipah virus (NiV) respectively (Table 1).<sup>6</sup>

Broadly, community transmission can be categorized into: 1) Clustered community transmission, where additional cases are from people whose tracing is impossible to known cases but are among the defined group such as cities, hovel or wide ranging events, where one can identify the growth of cases within specified

group in exponential pattern. 2) Widespread sustained community transmission, where additional cases are from diverse, non-linked groups and self-proliferating with

exponential growth of cases across these groups where most of the population of nation or territory are prone to the particular disease.<sup>7</sup>

**Table 1: History of pandemic.**

Virus and disease	Country of origin	Year of origin	Decline of outbreak
<b>Variola- Smallpox</b>	Egypt	1570 BC-1085 BC	19779
<b>H1N1 virus- Spanish flu</b>	Spain (Mexico)	1918	1919
<b>HIV- AIDS</b>	Republic of Congo, Africa	1981	2006
<b>Dengue virus- dengue fever</b>	Africa and South east Asia	1780	2017
<b>Nipah virus- Nipah virus infection</b>	Malaysia	1998	1999 (in Malaysia), 2018 (last case reported in India)
<b>H2N2 virus</b>	China	1957	1958
<b>H3N2 virus, Hong Kong flu</b>	China	1968	1970
<b>SARS-CoV-2, coronavirus infectious disease</b>	China (Wuhan)	2019	Ongoing

**Table 2: Details of various viruses.**

Virus	Scientific name	Taxonomy		
		Family	Genus	Species
<b>Smallpox virus</b>	Variola virus (VARV) <sup>10</sup>	Poxviridae	Orthopoxvirus	Variola major <sup>11</sup>
<b>Spanish flu</b>	H1N1 virus (Influenza A)	Orthomyxoviridae	Alphainfluenzavirus	Influenza A virus subtype H1N1
<b>HIV</b>	HIV-1, HIV-2	Retroviridae	Lentivirus	HIV-1, HIV-2
<b>Dengue virus</b>	DENV (1,2,3,4,5)	Flaviviridae	Flavivirus	Dengue virus
<b>Nipah virus</b>	Nipah henipavirus	Paramyxoviridae	Henipavirus	Nipah henipavirus
<b>H2N2 virus</b>	H2N2 virus (Influenza A)	Orthomyxoviridae	Alphainfluenzavirus	Influenza A virus subtype H2N2
<b>H3N2 virus</b>	Influenza A virus subtyoe H3N2	Orthomyxoviridae	Alphainfluenzavirus	Influenza A virus subtype H3N2
<b>Coronavirus (SARS-CoV-2)</b>	SARS-CoV-2	Coronaviridae	Betacoronavirus	Severe acute respiratory syndrome- related coronavirus

These all are challenges, but some are even much worse than others. No matter how well we are prepared, some storms take relatively a toll. Beyond study, investigations and evolution, we need a public wellbeing attitude that comprises far more than conscripting of overall plans, as numerous countries and states have done. We need a thorough operative plan of the best way to get over 12 to 24 months of a pandemic.<sup>8</sup>

This review includes detailed data regarding various viral pandemics. Analysing the history, clinical manifestation, pathogenesis, management and precautions of several viral pandemics which will promote and spread the awareness among the public as well as the healthcare system. The information was collected through computerized search from research article and various guidelines related to pandemics using various journal sites and health care organizations. “An epidemic arising over a very diverse area, crossing the global margins, and typically affecting a huge number of people” is defined as a pandemic.

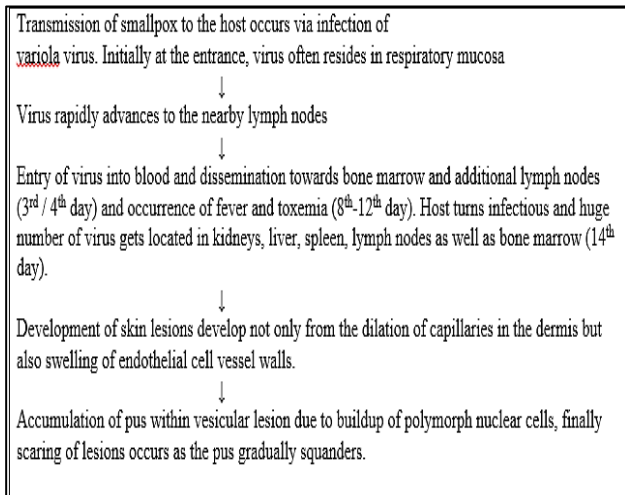
### SMALL POX

Smallpox is a severe, infectious, communicable disease caused by the variola virus (minor and major), belonging to the genus *Orthopoxvirus*, of Poxviridae family. Virologists have ventured that it advanced from an African rodent poxvirus 10 million years ago.<sup>16</sup> It is quite challenging to predict when exactly smallpox first infected humans, but proofs give idea that it may have first observed in the course of Neolithic age. Especially, in mummified Egyptians, Pharaoh Ramses V (d. 1157 BC), provided the first reliable indication of smallpox infection.<sup>17</sup>

### Clinical manifestation

PCR analysis helps for accurate determination of lesions under certain temperature. Early symptoms include-malaise (head and body aches), fever (101-104°F), vomiting (in some cases).

As the virus progresses following symptoms likely to develop- rash emerges as red spots turns into sores and burst rash observed on skin initiating from face progressing to arms and legs then hands and feet disseminating throughout the body within a day. On third day rash becomes bumps, fourth day bumps get loaded with fluid, fever relapses and doesn't subside until the bumps get peeled off.<sup>18</sup>



**Figure 1: Pathogenesis of small pox.**

### Mode of transmission

In variety of ways, smallpox is capable of spreading from person to person, among which transmission as a result of face to face contact for an extended period of time is the most common mode of transmission. Smallpox may also spread through direct contact with body fluids and contaminated objects. Through air or placental transmission can be considered as the rarest way by which smallpox gets transmitted.

### Stages of smallpox development

Stage I: Incubation Period, usually starting from 7 to 17 days (Not contagious). Stage II: Prodromal period starting from 2 to 4 days (sometimes contagious). Stage III: Early rash in about 4 days (Most contagious). Stage IV: Pustular rash observed after 5 days (Contagious). Stage V: Pustules and Scabs appear in about 5 days (Contagious). Stage VI: Resolving scabs within about 6 days (contagious).

### Treatment

Vaccines are available to protect the people from smallpox. At present, the smallpox vaccine is not compulsory for the common people as it has been wiped out. The ACAM2000 and APSV (i.e., replication-competent smallpox vaccines) can defend individuals from getting sick or the disease becomes less severe if received already or within seven days of coming in contact with the virus.

### Antiviral drugs

A drug called tecovirimat (TPOXX) have exhibited a prominent outcomes in preventing the progression of the virus in laboratory that is responsible for causing smallpox, which has been approved by the FDA on July 2018. It has been used in treating animals that had diseases like smallpox. Also, tecovirimat could also be used to treat adverse reactions from vaccinia vaccination under an investigational new drug (IND).

Cidofovir and brincidofovir has also shown results to stop the growth of the smallpox virus in laboratory tests. These have not been tried in people with smallpox infection, but have been tried in healthy people and in those with other viral infections. It has not been approved by FDA. It could still be used for certain unique scenarios including remote cases or during the course of an outburst under proper monitoring mechanism (like investigational new drug [IND] protocol or emergency use authorization).<sup>19</sup>

### SPANISH FLU

The most austere influenza outburst of the 20<sup>th</sup> century in terms of the numbers of deaths is the Spanish influenza pandemic of 1918-19 (Spanish flu) was among the most disastrous pandemics in history. It is caused by the virus that is transmitted through airborne respiratory secretions from person to person.

### Clinical manifestation

Primarily, epithelial cells of respiratory tract are targeted. Typical influenza syndrome includes fever, cough and general aches usually lasting from 3-7 days. Some of the prominent manifestation that led to hospitalization of younger children includes laryngotracheobronchitis, pneumonia and unexplained fever. Adults are more often observed with complications of bacterial pneumonia as well as worsening chronic pulmonary disease or congestive cardiac failure. Following are some of the rarest complications- myositis, various neuralgic disorders and Reye's syndrome.

### ASIAN FLU

In February 1957, after almost 40 years of H1N1 being the only influenza strain another influenza strain was spotted in the Yunnan Province of China.<sup>21</sup> This strain was found to be milder when compared to other two influenza strains. Even though virus was transmitting during summer, community wise transmission was restricted.

### Clinical manifestation

Initial symptoms include wobbly legs and a chill followed by prostration, sore throat, running nose and cough along with achy limb (adults), head (children), followed by high

fever. In most of the condition symptoms were mild and great recovery rate have been found after a period in bed with simple antipyretic measures. Complications were seen in around 3% of the cases with the mortality rate of 0.3%. Bronchitis and pneumonia makeup 50% of these, cerebro and cardiovascular disease account for remaining percentage.<sup>22</sup>

### HONG KONG FLU

Also called as ‘Mao flu’, arose in China in the winter of 1957 and spread rapidly worldwide starting from Hong Kong in April where about 2.5 lakh got infected, and by June over a million cases were observed in India. After a while it touched down in UK and by September in England, Wales and Scotland several cases were reported.<sup>23</sup>

#### Clinical manifestation

Principal findings among basic cases include malaise, fever, myalgia, cough, headache, coryza and sore throat. As per the report by the University of Singapore Health Service, some experienced atypical symptoms such as anorexia, nausea and ocular pain.<sup>24</sup>

### Mode of transmission of influenza viruses

Primarily transmitted from person to person through airborne respiratory secretion in the form of large respiratory droplets (>5 µm). Direct contact- touching hands (self-contamination), indirect contact-contaminated surfaces or objects (self-contamination), small particle aerosol (during aspiration or intubation). These travel only short distances usually 1 meter or less through the air.

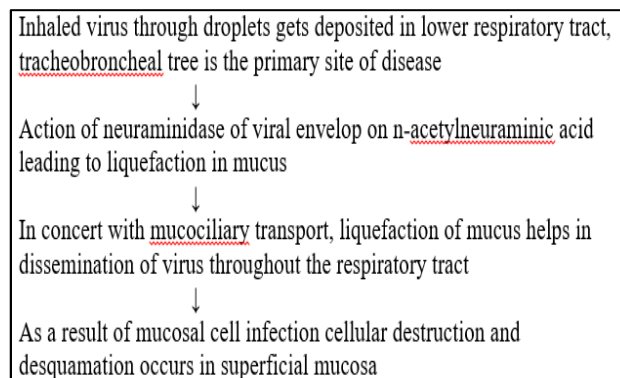


Figure 2: General pathogenesis of influenza viruses.

Table 3: Epidemiology and treatment.

Viral disease	Fatality rate	Mortality rate	Vaccination
<b>Smallpox</b>	Before vaccine- 7.6% (1 in 13 death) <sup>13</sup> After vaccine- <1%	Variola minor- 1% Variola major- 30%	Smallpox vaccine by Edward Jenner in 1796-Vaccinia (Ankara strain, City Board of Health Strain), double stranded DNA virus <sup>14</sup>
<b>Spanish flu</b>	>2.5%	50- 100 million worldwide	No vaccine
<b>AIDS</b>	100%	60%	No vaccine
<b>Dengue fever</b>		<1% (early detection), 2-5% (severe dengue when treated), 20% (when untreated) <sup>15</sup>	Dengvaxia (CYD-TDV) in 2015
<b>Nipah virus infection</b>	>70% (In India and Bangladesh), 40-75% (worldwide)	>75%	No vaccine
<b>Asian Flu</b>	0.67%	1.1 million	Influenza Virus vaccine, monovalent type A (Asian strain 5ml)
<b>Hong Kong flu</b>	0.5%	16.9%	NYMC X-203, NYMC X-203A, NYMC X-213, IDCDC- RG55C
<b>Coronavirus infectious disease</b>	1.52% (India), 0.1-25% in countries worldwide	3.4%	BNT162, mRNA-1273, Ad5-nCoV, AZD1222, CoronaVac, Covaxin, JNJ-78436735, NVX-CoV2373, Sputnik V

### ACQUIRED IMMUNO DEFICIENCY SYNDROME (AIDS)

HIV1 pandemic is a compound mixture of various epidemics within and among different countries as well as regions of world, effecting thousands of people leading to public health crisis. On estimation, around 38.6 million

people survived with HIV1 throughout the world whereas about 25 million have already died. In 2005, highest number of HIV1 cases (4.1 million) have been found and 2.8 million expired of AIDS. Based on their genetic structure, HIV1 viruses are grouped into 3 groups: M, N and O.<sup>25</sup>

**Clinical manifestations and opportunistic infections**

Fever (96%), lymphadenopathy (74%), pharyngitis and rash (70%), myalgia/arthralgia (54%), diarrhea and headache (32%), weight loss (13%), neurologic symptoms (12%), fungal infections; (oral candidiasis), Coccidioidomycosis, Cryptococcosis. Viral infections: encephalopathy, herpes simplex virus, histoplasmosis, Kaposi’s sarcoma. Bacterial infections: tuberculosis, pneumonia, Mycobacterium avium complex, Progressive multifocal leukoencephalopathy. Parasitic infection: toxoplasmosis.

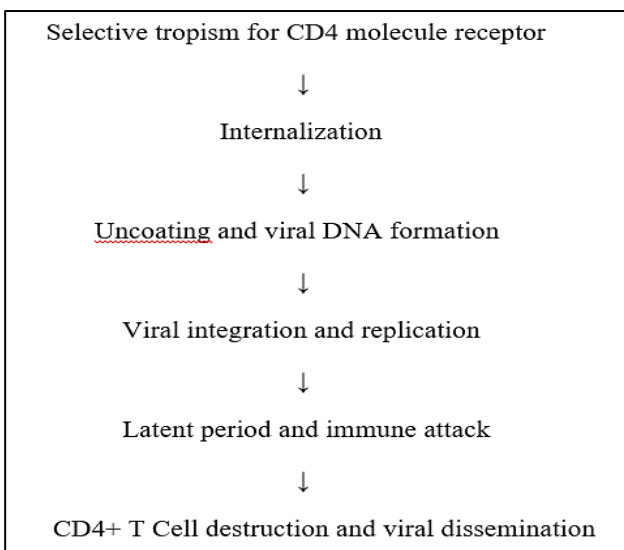
**CDC stages**

Stage 1: Acute HIV Infection. Stage 2: Asymptomatic HIV. Stage 3: Early symptomatic HIV. Stage 4: Late symptomatic HIV: A) Constitutional disease. B) Neurological disease. C) Secondary infection. C1- AIDS Defining. C2- Other infections. D) Secondary cancers. E) Other conditions

**Pathogenesis**

*Mode of transmission*

HIV is transmitted primarily via following routes: infected blood, semen, vaginal fluids, breast milk.



**Figure 3: Pathogenesis of AIDS.**

The majority of HIV transmission takes place through male to female transmission and the basis of viral spread on this transmission route is not known. Another common route of transmission is mother to child transmission.<sup>26</sup>

*Treatment*

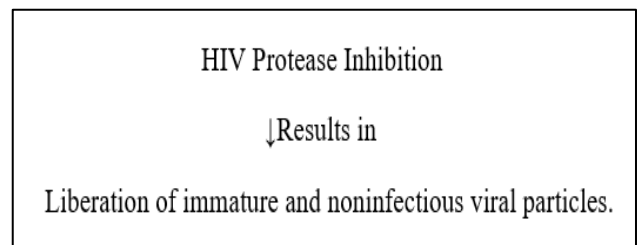
No cures exist for AIDS, but strict adherence to antiretroviral regimens can radically slow down disease’s advancement by keeping the viral load under control.

Effective management of HIV infection is possible using combination various available drugs. This method of treatment is collectively called as antiretroviral therapy.

**FDA approved HIV drugs**

*Reverse transcriptase inhibitors-* group of drugs which has a potential to bind and inhibit an enzyme called reverse transcriptase to interrupt the multiplication of HIV. There are two types of inhibitors: 1) Non-nucleoside reverse transcriptase inhibitors (NNRTI): First generation NNRTIs include Nevirapine, Delaviridine and Efavirenz which have poor resistance profile as well as low genetic barrier. Hence, development of new generations that is second generation NNRTIs were done including Etravirine and Rilpivirine. 2) Nucleoside reverse transcriptase inhibitors (NRTI): These drugs can be considered as ‘backbone’ of antiretroviral therapy (ART) regimens since past two decades. They selectively target HIV-1 reverse transcriptase enzyme and causes inhibition of viral RNA replication. These drugs donot go through phase I hepatic metabolism, making them devoid of drug-drug interactions. Examples include: Zidovudine, Stavudine and Festinavir (structural analogue of thymidine).<sup>27</sup>

*Protease inhibitors-* For the accurate assembly and production of HIV, regulation of HIV protease is extremely crucial. They effectively block the functioning of protease enzyme in both acutely as well as chronically HIV infected CD4 cells. Examples include lopinavir/ritonavir, indinavir, neflinavir and amprenavir.<sup>28</sup>



**Figure 4: Mechanism of action of protease inhibitors.**

*Fusion inhibitors-* A classic examples for this class of drugs are: Enfuvirtide which works by blocking HIV from getting into the CD4 cells of infected patients. Fusion inhibitors also work by obstructing the fusion of HIV particles with CD4 cells.<sup>29</sup>

*Chemokine receptors 5 antagonist-* They block chemokine receptor (CCR5) which are situated on CD4 cells. Maraviroc is an example of a CCR5 antagonist used in HIV treatment.<sup>30</sup>

*Integrase strand transfer inhibitors-* By acting integrase enzyme they avoid the integration of viral DNA into host genome of CD4 cells. Blocking of integrase enzyme prevents HIV from replicating. Examples: elvitegravir, raltegravir and dolutegravir.<sup>3</sup>

**Table 4: FDA approved four influenza antiviral drugs suggested by CDC for use against influenza viruses.**

Drug		Class	Dose and route of administration		Adverse effects
Generic name	Brand name		Paediatric	Adult	
<b>Peramivir</b>	Rapivab	Antiviral, Neuraminidase inhibitors	12mg/ kg i.v. as a single dose (2-12 years), 600 mg i.v. as a single dose ( $\geq 13$ years)	600 mg i.v. as a single dose	Neutrophils $< 1 \times 10^9/l$ , increased serum glucose ( $>160$ mg/dl), AST and ALT increased, constipation, insomnia, hypertension
<b>Zanamivir</b>	Relenza	Antiviral, Neuraminidase inhibitors	10 mg inhaled q 12 hours for 5 days, start within 2 days of symptom onset	10 mg inhaled q day for 10 days, start within 2 days of symptom onset. Community outbreaks: begin within 5 days of outbreak, may administer for up to 28 days.	Headache, throat/tonsil pain, cough, viral infection
<b>Oseltamivir</b>	Tamiflu	Antiviral, Neuraminidase inhibitors	75 mg PO q day for at least 10 days ( $\geq 13$ years), $<15$ kg: 30 mg PO q day for at least 10 days (1-12 years)	75 mg PO q 12 hours for 5 days	Abdominal pain, conjunctivitis, epistaxis, insomnia, ear disorder, vertigo
<b>Baloxavir Marboxil</b>	Xofluza	Antiviral, Endonucleus inhibitors	40 mg PO as a single dose (40-80 kg, $\geq 12$ years), $<12$ years: safety as efficacy not established	40 mg PO as a single dose (40-80 kg), $\geq 80$ kg: 80 mg PO as a single dose	Diarrhea, bronchitis, nasopharyngitis

Recent recommendations by WHO for antiretroviral therapy (ART)

**First-line ART:** Adults- Consists of two NRTIs and one NNRTI. Tenofovir disoproxil fumerate (TDF) + Lamivudine (3TC) or Emtricitabine (FTC) + Efavirenz (EFV).

Alternatively, 1) Zidovudine + 3TC + EFV. 2) AZT + 3TC + Nevirapine or. 3) TDF + 3TC + NVP.

**Pediatrics:** For patients  $<3$  years, initially given with protease inhibitors such as lopinavir/ritonavir, even under the exposure of NNRTI. For patients  $>3$  years, EFV is the best choice of NNRTI whereas NVP has been recognized as secondary option.

**Second-line ART:** Used when first line ART treatment miss the mark. Adults- Primarily two NRTIs and Ritonavir- boosted PI, AZT and 3TC can be considered as a recommended option.

**Pediatrics:**  $<3$  years, first line ART is recommended to continue even when it fails. No change in treatment is recommended. Alternative to this some of the key steps should be taken in order to enhance adherence to the ART regimen. It consists of one NNRTI and two NRTIs.

Recommended option is AZT + 3TC in case ABC or TDF + 3TC fails.

**Third-line ART:** Includes integrase inhibitors together with second generation NNRTIs as well as PIs.<sup>32</sup>

## CORONAVIRUS INFECTIOUS DISEASE

Wuhan, China witnessed the first ever outbreak of novel coronavirus infection in December 2019. Even after the launch of an emergency response during the initial stage of outbreak, the infection spontaneously disseminated to metropolitan areas of China as well as worldwide. It is caused by newly discovered coronavirus strain (SARS-CoV-2). These group of RNA viruses are morphologically resemble a crown like structure that primarily causes the infections either in nose, sinus or in upper throat.<sup>33</sup>

### Clinical manifestation

Based on severity, authors of Chinese CDC report divided the clinical manifestations of the disease as mild, severe and critical. Most common symptoms include cough, breathlessness, dry mouth, and sore throat.

Mild disease includes non-pneumonia and mild pneumonia which occurred in around 81% of cases.

Severe conditions include respiratory frequency less than 30 per minutes, dyspnea, blood oxygen saturation greater than 93%, PaO<sub>2</sub>/FiO<sub>2</sub> ratio or P/F and the percentage of oxygen supplied greater than 300, and/or lung infiltrate less than 50% within 1-2 days; around 14% of cases are found with above data.

Critical disease include approximately 5% of cases that are found with critical diseases like septic shock, respiratory failure, and/ or multiple organ dysfunction or failure.<sup>34</sup>

### **Mode of transmission**

Initial cases of corona virus infectious disease were associated with direct exposure to Huanan Seafood Wholesale Market. The main mechanism was assumed as animal to human transmission which was not proved in subsequent cases as the viral spread was not seen from animals to humans. Hence, it was clinched that the virus is transmitted from human to human. The most repeated source of COVID-19 transmission is considered to be symptomatic people. As there are chances of transmission prior to symptoms, and hence individual who stay asymptomatic could spread virus, the best way to combat this pandemic is remaining isolated. As seen in other respiratory pathogens, including rhinovirus and flu, it was assumed that spreading of virus occur from coughing and sneezing through respiratory droplets of particle size greater than 5-10 µm in diameter. 80% of COVID-19 transmissions are associated with pre and asymptomatic individuals. The transmission is initially restricted to family members, healthcare professionals and other closed contacts around 6 feet, 1.8 meters. Details regarding duration of contamination on objects and surfaces are as follows: Plastic: 2-3 days, Stainless steel: 2-3 days, Cardboard: 1 day, Copper: 4 hours.<sup>35</sup>

### **Pathogenesis**

The mechanism by which SARS-CoV-2 produces symptoms seems to be complex. +ssRNA of around length 30kb embedded in a genomic structure of virus. It comprised of 5'-cap and 3'-poly-A tail. Beginning from viral RNA the production of poly protein 1a/1ab in the host is recognized. Organization of replication-transcription complex (RCT) in double membrane vesicles and through the production of sub genomic RNA sequences is the modes via which the process of transcription occurs. Transcription regulatory sequences which are situated within the open reading frames (ORF), work as templates for sub genomic mRNAs. Generally, in a typical genome of coronavirus at least 6 ORFs may be present among which ORF 1a and 1b directs the synthesis of pp1a and pp1ab polypeptides which are processed by proteases, chymotrypsin-like protease and main protease. Among the structural components of viruses, two

subunits S1 and S2 are embedded within glycoproteins. Homo trimers of s proteins makeup the spikes on the surface of virus directing the link to host receptors. Receptor binding domain (RBD) represents a binding site for binding site for human angiotensin converting enzyme 2 receptor (ACE 2 receptor). Polybasic site allows the functional processing of ACE 2 by an enzyme called protease which allows the acquaintance of fusion sequences and thereby virus and cell membranes get fused.<sup>36</sup>

### **Treatment**

Currently, there is no specific antiviral treatment or vaccine found for COVID-19. Symptomatic treatment is encouraged and oxygen therapy is considered as first step against respiratory impairment. In case of respiratory failure refractory to oxygen therapy non-invasive (NIV) and invasive mechanical ventilation. For complicated forms of disease intensive care is mandatory.

*O<sub>2</sub> fast challenge-* In a patient with oxygen saturation <93-94% (If COPD, 88-90%) or dyspnea, administration of oxygen by a 40% venturi mask must be undertaken. Reassessment is done after 5-10 min to determine any improvement of clinical features. Treatment is continued in case of improvement whereas noninvasive treatment is chosen if the condition is worsening.<sup>37</sup>

*High flow nasal oxygen (HFNO)-* Generally indicated when it is hard to maintain SpO<sub>2</sub> >92% and adjustment is done according to the clinical response by supplying 30-40 litres/minute and FiO<sub>2</sub> around 50-60%. If no improvement is seen after an hour when given with >50 litres/minute and FiO<sub>2</sub>>70%, then switch to NIV. HFNO can also be considered to break CPAP and also for fiberoptic tracheal intubation in critically ill patients. HFNO is contraindicated in hypercapnic patients.

*Non-invasive ventilation and continuous positive airway pressure-* Begins with 8-10 cm H<sub>2</sub>O and FiO<sub>2</sub> 60%. NIV starts with PEEP 5 cm H<sub>2</sub>O checking the tolerance of patient and bring to 8-10cm H<sub>2</sub>O, FiO<sub>2</sub> 60%, PS 8-10 cm H<sub>2</sub>O.

It is not recommended to make any changes in first day, at least after 4-6 hours detach for maximum 1 hour only stabilized. Small quantities of fluid are allowed to intake during night.<sup>38</sup>

*Antiviral agents-* Even though no antiretroviral treatments have been approved, several approaches have been put forward like lopinavir/ritonavir, 400/100 mg orally every 12 hours. Preclinical studies recommended that, an inhibitor of RNA polymerase with in vitro activities against multiple RNA viruses called remdesivir could be effective for prophylaxis as well as therapy of coronavirus infection.<sup>39</sup>

Several anti-flu medications like oseltamivir have been recommended for COVID-19 treatment. Favipiravir, another anti-flu drug which proved to be efficacious against SARS-CoV-2 invitro. In a retrospective investigation a broad spectrum antiviral called arbidol was shown to be a good agent which not only can improve discharging rate but also decrease mortality rate of Covid-19 patients.<sup>40</sup>

*Immunomodulatory drugs*- Initially chloroquine, 500 mg, every 12 hours and hydroxychloroquine (HCQ), 200 mg, every 12 hours were recommended as immunomodulatory therapy. These drugs especially HCQ was considerably associated with reduction of viral load which was boosted by macrolide antibiotic, azithromycin.<sup>41</sup>

*Serotherapy*- From the blood of healed individuals antibodies are taken and are studied for therapeutic option.

*Inflammation inhibitors*- A humanized IgG1 monoclonal antibody, directed against IL-6 receptors called as tocilizumab is investigated by an Italian foundation. Other interleukin receptor antagonist/antibody namely sarilumab and anakinra used to treat auto inflammatory disorders such as adult-onset stills disease, systemic onset juvenile idiopathic arthritis and familial Mediterranean fever.<sup>42</sup>

## PRECAUTIONS

Most of the viral pandemics mentioned above spread through prolonged face to face contact via droplets expelled from the nose and mouth of a patient, generally by coughing. A disease like smallpox is also transmitted through contact with materials from smallpox scabs. Following are some of the predominant measures that are mandatory to follow in order to get through these pandemics.<sup>43</sup>

*Usage of person protective equipment (PPE)*: It is necessary that all the staffs of healthcare team as well as visitors or any other person coming in close contact with the patient to follow standard, contact as well as airborne precautions regardless of vaccination status.

*Criteria for PPE*: Disposable gown and gloves. NIOSH certified N95 filtering disposable respirator. Eye protections such as face shields are mandatory in case of medical procedures which may lead to splashing or spraying of patients body fluids.

Before exiting patient's room it is required to remove all PPE, except for N95 respirator. After removal of gloves, the staff members must wash his/her hands either with soap or alcohol based hand sanitizer.<sup>44</sup>

*Disinfected and sterilized environmental surfaces*: The nature and magnitude of surface contamination will recite

the level of disinfection either as low or intermediate, needed to make the surface safe to handle or use. Fumigation isn't a relying method of disinfecting rooms, facilities or vehicles containing variola virus.<sup>45</sup>

*Disposable medical apparatuses and patient care devices*: 'Category A' wastes are imparted with certain guidelines called waste management guidelines which are of prime importance in maintaining overall hygiene of entire healthcare team as well as public.

*High efficiency particulate air (HEPA) filters*: Usage of vacuum cleaner installed with a high efficiency particulate air filter for cleaning carpeted floors or upholstered furniture.

Disposal of all waste contaminated with viruses is considered to be category A infectious substance which is regulated as hazardous materials under the US Department of transportation containing set of regulations which require special packaging hazardous materials prior to transport.<sup>46</sup>

## CONCLUSION

Rigorous understanding of various pandemics or outbreaks and consequences of their community spread across the globe till date along with their etiology as well as primary root of origin is crucial. To determine the impact of various communicable diseases on nation's economic status, to explore the role of healthcare expenditures in bringing down various pandemics, to notice any fluctuations in poverty rates and population density due to different pandemics, to understand the importance of individual's behavioural change by strengthening oneself psychologically for combating against various possible outbreaks that may occur in most unpredictable manner and most importantly helping Government of our nation to take commendable, stringent and most accurate decisions for the purpose of all round development of a country including key areas such as economy and health status.

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*Ethical approval*: Not required

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