



## COVID-19: A Bitter Truth

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### **Abstract:**

*The COVID-19 (Coronavirus Disease-19) is extremely contagious and quickly spreadable pathogenic viral infection caused by SARS-CoV-2, a virus belongs to coronavirus family member. It was appeared abruptly in Wuhan, China; transmitted possibly from bat to human followed by human to human and now becomes pandemic. The intermediate stage of transmission is not known but becomes a global challenge to stop the spread of virus. The best way to avoid the chain of viral spread is suggested as isolation. Though, mutagenic strains of this virus has been observed, the genome of virus has been sequenced that helps in development of viral diagnosis kit. Vaccines has been developed in the vast genomic era and now the world is moving towards direct human vaccine trial. The sensitivity of diagnostic kits, development of antiviral drugs and vaccines can save the life. This review is focused on overall knowledge of viral origin, their genetics, structure, diagnosis, precautions and possible therapy currently developed or under developmental progress by scientist.*

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**Key words:** COVID-19, SARS, virus, vaccine, diagnosis.

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### **1. Introduction**

Infectious viral diseases continue to appear as a serious health concern on global basis. Several viral epidemics such as the severe acute respiratory syndrome coronavirus in 2002-03, H1N1 influenza in 2009, Middle East respiratory syndrome coronavirus in 2012 has been observed in last two decades. The illness is now emerged in 2019 as a novel highly infectious virus belonging to the coronavirus (CoV) family. Coronavirus disease 2019 (COVID-19) is an infectious disease caused by SARS-CoV-2, a modified strain of coronavirus. The disease current outbreak is recognized as a pandemic by World Health Organization (WHO). Originated from the bat, intermediate source in origin and their transfer to humans is unclear. The epicenter of COVID-19 was Wuhan, China; however, it is now spread all over the world and had caused more than 0.12 million deaths and still in continuation exponentially. There is no clinically approved vaccine and antiviral drug available as permanent cure / remedy as of now, direct human clinical trials has been preceded by some countries. Although few research organizations had demanded the credit of identified genome sequence but the report still under consideration. Observing the panic pandemic effect of COVID-19, we have attempted a review on overall information about the origin, structure, taxonomy, transmission, epidemiology, diagnostic procedure and possibilities of treatment to manage with this viral outbreak.

### **2. History**

Coronaviruses being zoonotic in origin are found to be responsible for infection spread in many animal species such as pig, cat, rat, mouse, camel, bat and chicken including a mammalian transmission to humans also. Although several known coronaviruses are mingled into the animals that have not infected humans. In the detailed study found SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to humans (Susan et al., 2005).

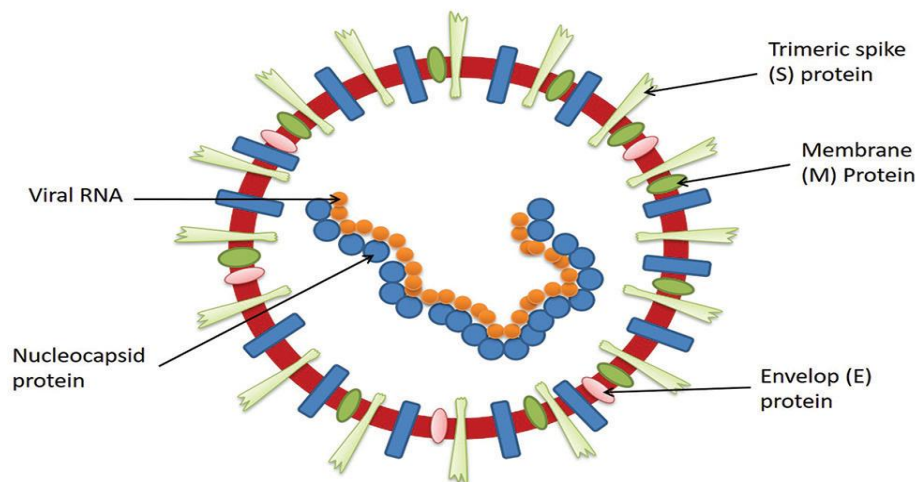
More than 50 years ago, information about the Corona viruses had been described for their prototype of murine coronavirus strain JHM which was first isolated in 1949 by Bailey et al., (1949).

Coronaviruses (CoVs) are family of viruses, initially causing an illness with an expression of myriad symptoms ranging from the common cold to ranging more too severe diseases like Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-CoV) (Cheever et al., 1949).

### 3. Structure of Corona Virus

Coronaviruses (CoVs) containing single + sense strand RNA having a genome size ranging between 26.2 to 31.7 kb, whose structure is coated with a small integral membrane protein envelope (Yang et al., 2006). Corona viruses are pleomorphic or spherical shape in nature, and it is characterized by bears club spike shaped projections of (S) glycoproteins on its surface (diameter 80–120 nm) as described by Hilgenfeld (2014). Among all the RNA viruses, CoV containing largest genome in ranges from 26.2 to 31.7 kb (Belouzard et al., 2012), can give rise to new strains with alteration in virulence (Hilgenfeld, 2014). Among seven total known strains of human CoVs, which include 229E, NL63, OC43, HKU1, Middle East respiratory syndrome or MERS-CoV, severe acute respiratory syndrome or SARS-CoV, and 2019-nCoV novel coronavirus, which are directly involved for the infection of respiratory tract (both lower and upper respiratory tract) exhibits a range of symptoms like common cold, pneumonia, bronchiolitis, rhinitis, pharyngitis, sinusitis, and other system symptoms such as occasional watery diarrhea etc (Chang et al., 2016; Paules et al., 2020).

Among these seven strains, three strains are highly pathogenic in nature (SARS-CoV, MERS-CoV and 2019-nCoV), which had caused endemic of severe CoV disease (Paules et al., 2020). Generally reservoir of SARS-CoV is unknown, but hypothetically bats are one of the reasons to spread SARS-CoV on other hand camels are carriers of MERS (Middle East Respiratory Syndrome) (Saifet al., 2004; Al-Osail et al., 2017).



**Fig 1. Structure of Human Corona-virus** (source: Prajapat et al., 2020; Shereen et al., 2020)

### 4. Taxonomy

“Corona virus” name was described in 1968, for the morphological structure of “corona”-like or crown-like shape was observed by using electron microscope (Tyrrel et al., 1968). According to International Committee on the Taxonomy of Viruses, Corona virus belongs to the Coronaviridae family. Recently, at the 10<sup>th</sup> International Nidovirus Symposium in Colorado Springs at June 2005, Coronaviridae family has been divided into two subfamilies, as the corona viruses and toro viruses, probable causal agent of enteric diseases in cattle and possibly in humans (Cowley et al., 2000; Enjuanes et al., 2000).

According to the groups and serological cross-reactivity corona viruses are divided into three genera (I to III) by McIntosh (1974). Genome sequence analysis has confirmed that, Group I corona viruses are animal pathogens, such as TGEV of the pig, PEDV or porcine epidemic diarrhea virus, HCoV-229E or human corona viruses and HKU1, FIPV or feline infectious peritonitis virus which causes respiratory infections. Group II includes veterinary relevance pathogens, like equine corona virus, porcine hemagglutinating encephalomyelitis virus, BCoV as well as human corona viruses like HCoV-229E. Group II virus infects rats and mice and had found to cause diseases such as enteric disease, encephalitis, chronic demyelination, hepatitis and respiratory disease etc. Some controversies regarding SARS-CoV infection, defines it as a new group of corona viruses or a distant member of group II, (Goebel et al., 2004; Gorbalenya et al., 2004).

While, Group III includes only avian corona viruses, such as turkey coronavirus, IBV and pheasant coronavirus (Susan et al., 2005; Cavanagh et al., 2002). Through reverse transcription-PCR (RT-PCR), coronavirus sequences have been detected in the graylag goose (*Anseranser*), mallard (*Anasplatyrhynchos*) and feral pigeon (*Columbia livia*) by Jonassen et al., (2005).

### 5. Novel Corona Virus

The newly identified strain of human coronavirus fooled by it's an initial spread in Wuhan city, China at December 2019 had caused thousands of cases and deaths. COVID-19 is the disease caused by the new virus SARS-CoV-2. According to the prediction of Vincent et al., (2007), Severe Acute Respiratory Syndrome (SARS) corona virus (SARS-CoV) is a novel virus that had caused the first major pandemic problem to the whole world (Drosten et al., 2003; Ksiazek et al., 2003 & Peiris et al.,2003).

Southern China has led to an increase of he spread in disease, due to the demand of animal proteins and exotic game food animals such as civets leading to a large numbers and varieties of wild animals, in an overcrowded cages and lack of biosecurity measures in wet markets. Novel virus could be transmitted from animals to human and now virus is having the capacity to transmit human-to-human (Webster, 2004; Woo et al., 2006). Initially World Health Organization (WHO) gives the name of corona virus is 2019-novel coronavirus (2019-nCoV) on 12 January 2020, After that, WHO had officially announced the name of the disease as coronavirus disease 2019 (COVID-19) besides, Corona virus Study Group (CSG) of the International Committee proposed a name to the new coronavirusas SARS-CoV-2, both being issued on 11 February 2020 by Yan et al. (2020). As of 15<sup>th</sup> April 2020, a total of 1,9,14,916 confirmed cases of COVID-19 and 1,23,010 deaths at globally have been confirmed (5020) as per WHO report-85 in Coronavirus disease 2019 (COVID-19).

### 6. Entry Mechanism of Coronavirus to Human

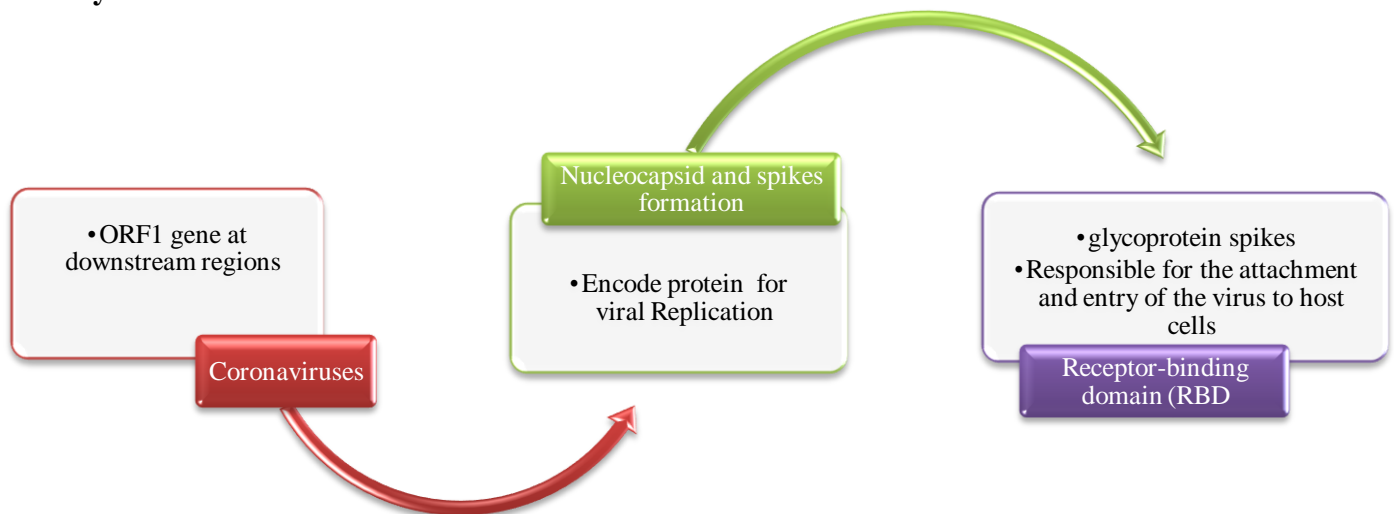
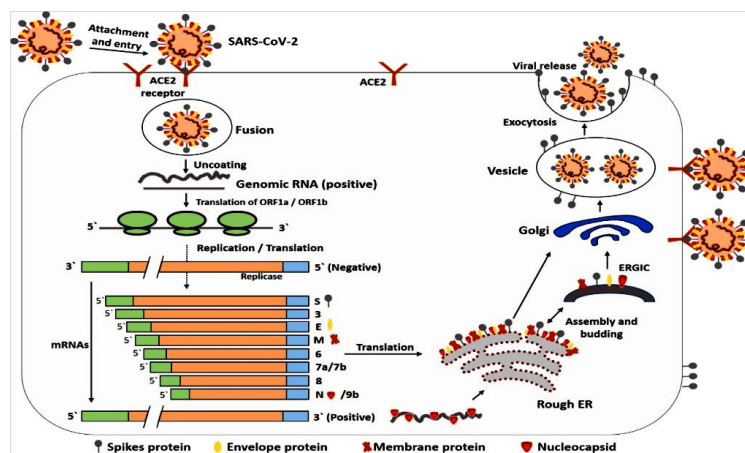


Fig 2. Important Stages of route of infection in human by Coronavirus



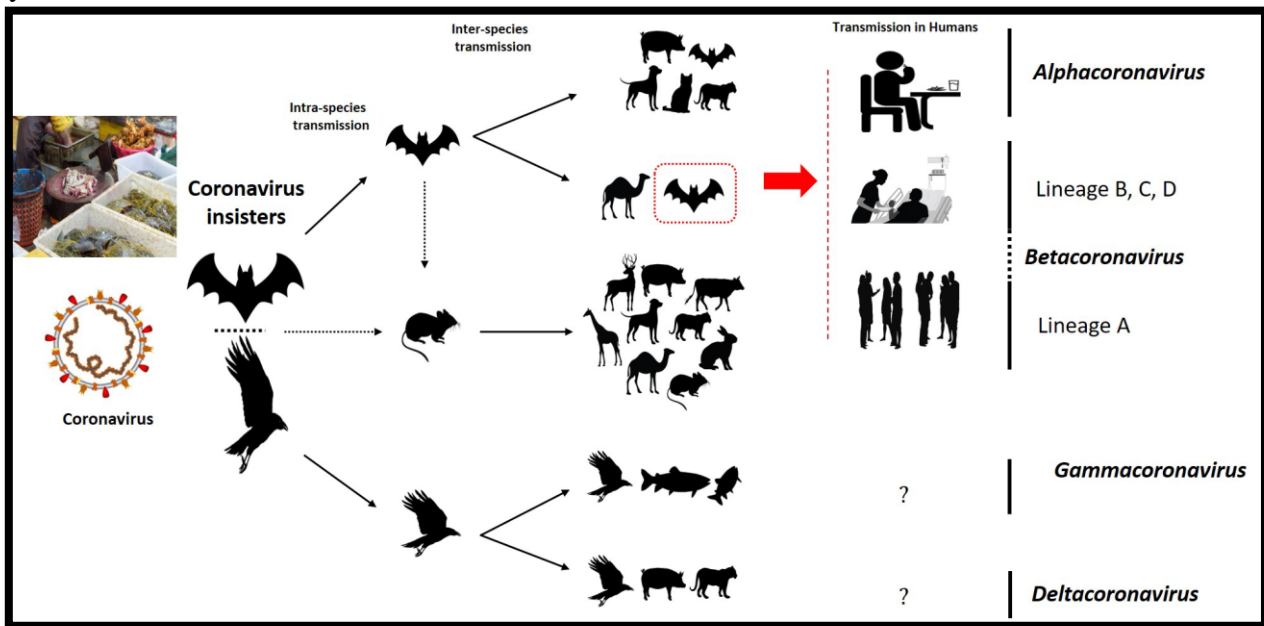
**Fig 3. The life cycle of SARS-CoV-2 in host cells** (source: Shereen et al., 2020)

(Note: ACE2, angiotensin-converting enzyme 2; ER, endoplasmic reticulum; ERGIC, ER–Golgi intermediate compartment).

SARS-CoV-2 possesses the typical coronavirus structure with spike protein and it also express other nucleoproteins, polyproteins, and membrane proteins, such as RNA polymerase, 3-chymotrypsin-like protease, papain-like protease, helicase, glycoprotein, and accessory proteins (Wu et al., 2020; Zhou et al., 2020). The life cycle begins when S- protein binds to the cellular receptor ACE2. Receptor binding occurs, S protein changes and fused with the viral envelope fusion of cell membrane through the endosomal pathway. After the fusion SARS-CoV2 releases RNA into the host cell. Then RNA translation take place into viral replicase polyproteins pp1a and pp1ab, and it cleaved into small products by viral proteinases. Then sub genomic mRNAs sequences have been produced by discontinuous transcription and it translated into whole viral proteins. (Xu et al., 2020; Raj et al., 2013) Genome RNA and viral protein together made assembly with virions in the Golgi body and Endoplasmic Reticulum and then transported through vesicles and released out of the cell (Fig.2 and Fig.3).

### 7. Transmission of Corona Virus from Animal to Human

Fig. 4 represents the mode of transmission of animal to human. Basically  $\alpha$  and  $\beta$  coronaviruses have the ability to infect humans. Generally, the cave animals like bats carries corona virus in their body they are the reservoirs. Whenever human being consume the infected animals as a source of food as they are the carrier of corona-virus is the major cause of human transmission by animals. When the infected person gets close contact with an another person, the virus is further transmitted to healthy human (Shereen et al., 2020) and the cycle continues.

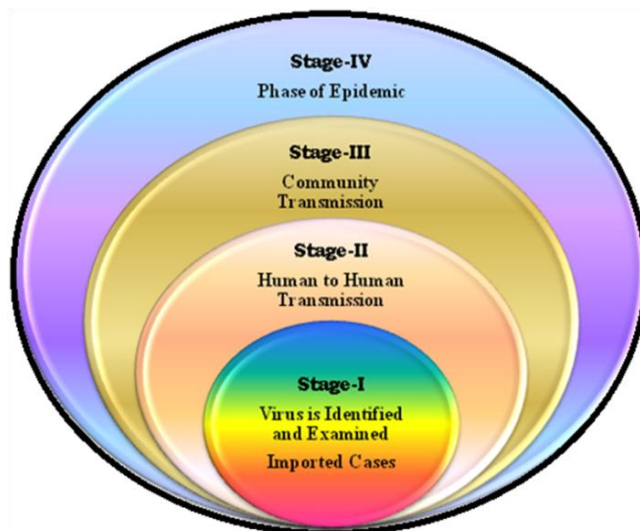


**Fig4. Mode of Transmission of Corona Virus from Animal to Human**  
(source: Shereen et al., 2020)

### 8. Pathogenesis of Pandemic Novel Coronavirus

The term transmission refers to the transmission of microorganisms from one individual to another uninfected individual, either through droplets or direct contact or through indirect transmission such as surface contamination.





**Fig 5. Phases of Coronavirus Infection**

Fig. 5 represents that, the novel Coronavirus has four stages of transmission of disease spread to humans and worldwide. According to the WHO guideline four phases are as follows:

**Stage – I** First stage comprises of an appearance (Sporadic cases) of disease through people who has travel history, with everyone contained, traced their sources, and no local spread from who is affected. The number of infection is quite low at this phase.

**Stage- II** Second stage (Clusters of cases) is the local transmission, when those who were infectious and having a travel history, spread the virus to their family or close friends. At this stage, every person who came in contact with the infectious person would be traced and isolated.

**Stage - III** This stage is comprised of community transmission & in these period infections occurs in public and the source of a virus cannot be traced. At this stage, complete lockdown become important because random members of the community infection occur and start developing the disease.

**Stage- IV** In the final phase, the disease becomes epidemic in some countries such as China, America and Italy with occurring large numbers of infections and a growing number of deaths with no end. It is then considered to be endemic or now pandemic to the region.

## **6. Symptoms Involved in Novel COVID-19 Infection**

According to the COVID-19 Resources from Mayo Clinic using its expertise to address the COVID -19 Pandemic is might be appeared 2 to 14 days after exposure of infected person and can include: Fever, Cough, Shortness of breath or difficulty breathing, Tiredness, Aches, Sore Throat, Runny Nose, Headache, Diarrhea and Vomiting, some of the people experienced the loss of smell or taste also.

## **7. Current Scenario of Incidence Rate and Death Toll Pandemic Coronavirus around the World and in India**

### **7.1 World Wide Pandemic Cases Overview**

According to the report of Coronavirus disease 2019 (COVID-19) Situation Report – 83 by World Health Organization, (2020) as is effective on 12<sup>th</sup> April 2020, newly arising cases and total death case has been mentioned at global level. Table 1 & Fig. 6 have shown records around the world about confirmed, new and death cases arisen in the countries that are entered into local and community transmission of novel Coronavirus infection.

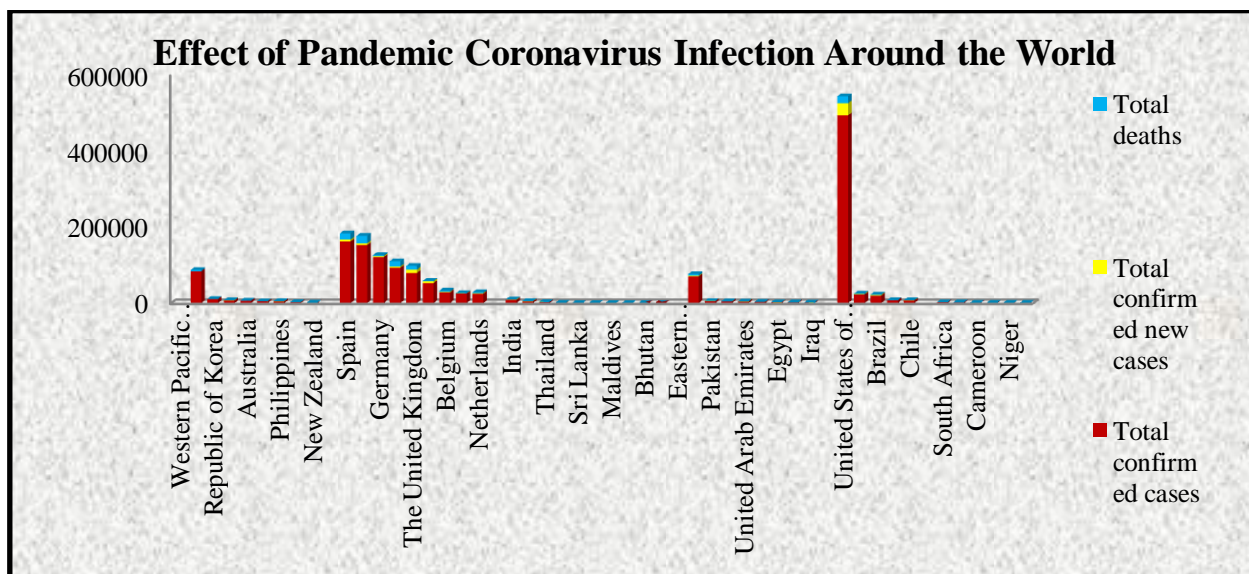
**Table 1: The Numerical Data of WHO by 12<sup>th</sup> April of Confirm, New Case & Death Rate by Pandemic Coronavirus around the World**

Reporting Territory/Area	Country/	Total cases	confirmed	Total confirmed new cases	Total deaths
<b>Western Pacific Region</b>					
	China	83482		113	3349
	Republic of Korea	10512		32	214
	Japan	6748		743	98
	Australia	6289		51	57
	Malaysia	4530		184	73
	Philippines	4428		233	247
	Singapore	2299		191	8
	New Zealand	1049		14	4
<b>European Region</b>					
	Spain	161852		4830	16353
	Italy	152271		4694	19470
	Germany	120479		2821	2673
	France	92787		3104	13814
	The United Kingdom	78995		8719	9875
	Turkey	52167		5138	1101
	Belgium	28018		1351	3346
	Switzerland	24820		592	831
	Netherlands	24413		1316	2643
<b>South-East Asia Region</b>					
	India	8356		909	273
	Indonesia	4241		729	373
	Thailand	2551		33	38
	Bangladesh	621		197	34
	Sri Lanka	199		2	7
	Myanmar	38		10	3
	Maldives	19		0	0
	Nepal	9		0	0
	Bhutan	5		0	0
	Timor-Leste	2		0	0
<b>Eastern Mediterranean Region</b>					
	Iran (Islamic Republic of)	70029		1837	4357
	Pakistan	5038		250	86
	Saudi Arabia	4033		382	52
	United Arab Emirates	3736		376	20
	Qatar	2728		216	6
	Egypt	1939		145	146
	Morocco	1545		97	111
	Iraq	1318		38	72
<b>Region of the Americas</b>					
	United States of America	492881		31606	18516
	Canada	22544		1318	600
	Brazil	19638		1781	1056
	Ecuador	7257		96	315
	Chile	6927		426	73

**African Region**

South Africa	2028	25	25
Algeria	1825	64	275
Cameroon	803	0	10
Côte d’Ivoire	533	53	4
Niger	491	53	11
Burkina Faso	443	0	19

(Note: Reprinted from Novel Coronavirus (2019-nCoV) situation reports-83 by WHO (2020, April 12). Retrieved from <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200412-sitrep-83-covid-19.pdf>).



**Fig 6. Effect of Pandemic Coronavirus Infection around the World**

(Note: The graph adapted from Novel Coronavirus (2019-nCoV) situation reports-83 by WHO (2020, April 12). Retrieved from <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200412-sitrep-83-covid-19.pdf>).

**7.2 Overview of pandemic corona outbreak in India**

In the present investigation of Confirm/ Active/ Recovered/ Deceased Coronavirus pandemic cases which have been recorded by official website of CORONA updates, report is extracted at 13<sup>th</sup> April, 2020. Table 2 and Fig. 7 & 8 have been displayed tabulated and graphical information about the pandemic effect of novel Coronavirus in India.

**Table 2: The Numerical Data at 13<sup>th</sup> April 2020 by Coronavirus Tracker of Confirm/ Active/ Recovered/ Deceased Pandemic Coronavirus Cases in India**

State/UT	CINFMD	ACTV	RCVRD	DCSD
Maharashtra	2334	1957	217	160
Delhi	1510	1451	31	28
Tamil Nadu	1173	1104	58	11
Rajasthan	897	765	121	11
Madhya Pradesh	614	513	51	50
Telangana	592	472	103	17
Gujarat	572	492	54	26
Uttar Pradesh	558	504	49	5
Andhra Pradesh	439	420	12	7
Kerala	378	179	198	2

Jammu & Kashmir	270	250	16	4
Karnataka	247	180	60	7
Haryana	196	142	51	3
Punjab	176	139	25	12
West Bengal	152	116	29	7
Bihar	66	37	28	1
Odisha	55	41	13	1
Uttarakhand	35	28	7	0
Himachal Pradesh	32	18	12	2
Chhattisgarh	31	21	10	0
Assam	30	29	0	1
Jharkhand	24	22	0	2
Chandigarh	21	14	7	0
Ladakh	17	5	12	0
Andaman And Nicobar Island	11	1	10	0
Goa	7	2	5	0
Puducherry	7	6	1	0
Manipur	2	1	1	0
Tripura	2	2	0	0
Arunachal Pradesh	1	1	0	0
Dadra And Nagar Haveli	1	1	0	0
Mizoram	1	1	0	0
Nagaland	1	1	0	0

Note: CINFMD- Confirm, ACTV- Active, RCVRD- Recovered, DCSD- Deceased reprinted from Corona Dashboard, [www.covid19india.org](http://www.covid19india.org).

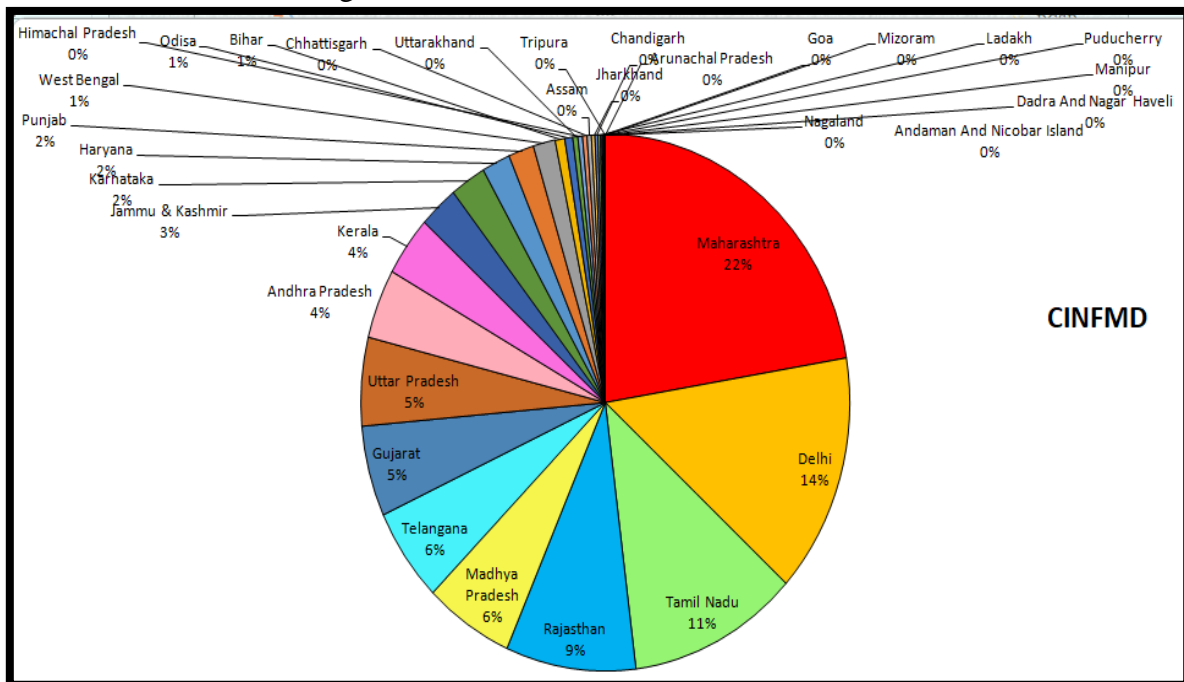
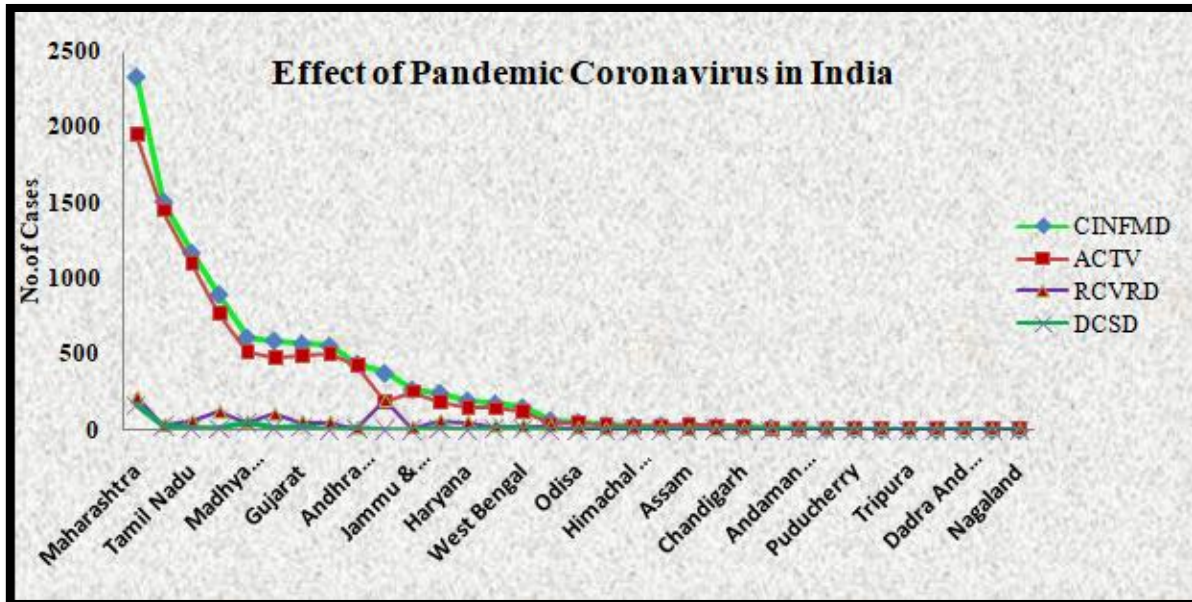


Fig 7. Geographical Percentage of Confirm Cases in Pandemic Coronavirus in India from Corona Dashboard, [www.covid19india.org](http://www.covid19india.org)





**Fig 8. Effect of Total Confirmed/ Active/ Recovered/ Deceased Cases in Pandemic Coronavirus in India from Corona Dashboard, www.covid19india.org**

### 8. Laboratory Diagnosis

At present myriad types of diagnostic approaches including in vitro (serological, biochemical etc) and in silico (molecular level e.g. PCR), kit based are under consideration and still many are under progress of trial and research. Some of them are summarized as follows:

The samples taken for the study are both naso and oro pharyngeal either individually or in combined manner to enhance the yield in quantity for smooth diagnosis (Tang et al., 2020).

### 9. Antigen Detection

1. Virus (Ag) in respiratory epithelial cells it has been detected by the monoclonal antibody through ELISA and IF tests. (Xiang et al., 2020).
2. Virus (Ag) in respiratory epithelial cells by Respiratory Secretions and to detection has been done by using stool specimen. Finally, the entire test is carried out by Electron Microscopy (Gui et al., 2017).
3. Virus (Ag) in RNA Detection nasal swabs, pharyngeal swabs, and stool specimen, blood sample has been tested through RT-PCR by novel signature sequence/ primer has been developed by china.
4. Lateral flow antigen detection as point of care test also paved the way to combat the rush of sample collection and patients visits in lab creating nuisance (Xiang et al., 2020).

### 10. Antibody based Serological Assays

Immunoassays employing Ag-Ab interaction using mAbs for detection of viral antigen in clinical sample or kateral flow assay in form of a dipstick encased cassette which captured a reagent (in two forms a. mAb directed at a viral antigen or b. a viral antigen that is recognized by patients' antibodies) get immobilized on specific sites of nitrocellulose membrane matrix and at definite locations of mAbs detector which recognize the antigen target. A colored line a positive response was indicated similar as pregnancy detection kit based assay (Sheridan,2020).

### 11. Gene level tests

PCR (RT-PCR) by WHO, in January, 2020 with a rapid diagnosis (4-6 hrs) followed by Central of Disease Control in month of February,2020 and leading companies National and International level like Roche Diagnostics, Thermo Fisher Scientific, Qiagen (soon to be acquired by Thermo Fisher) and Quest Diagnostics are coming as front runner to reach the target of reduction in time lapse of diagnosis with more rapidity.

## 12. First Indian Manufacture CoViD-19 Test Kit

The first made-in-India test kit for CoViD-19 developed by Pune-based molecular diagnostics company Mylab Discovery Solutions Pvt Ltd has received commercial approval from the India FDA/Central Drugs Standard Control Organization (CDSCO). This kit took only six weeks to develop the 'Mylab PathoDetect COVID-19 Qualitative PCR kit'. This kit achieved 100% specificity and sensitivity.

Currently a combination of diagnostics and apps in smart phones (e.g. "Aarogya setu") are also in the front line action to provide greater communication and surveillance (Udugama et al., 2020; Ministry of Health and Family Welfare, 2020).

## 13. Treatment for Pandemic Coronavirus

Currently there are first kind of therapeutic targets in use (Prajapat et al., 2020) and few are in research and clinical trials track waiting to be launched in market by FDA approval. Some of the detailing regarding this is as follows:

## 14. Vaccines for CoViD-19 in the Pipeline

- For the treatment to infection of CoViD-19, there are two vaccines in the pipeline against SARS-CoV-2.
- mRNA based vaccine prepared by the US National Institute of Allergy and Infectious Disease that is under phase 1 trail. Very soon mRNA based vaccine sample prepared by Stermirna Therapeutics will be available.
- INO-4800-DNA based vaccine available for human testing.
- Chinese Centre for Disease Control and Prevention (CDC) working on the development of an infected virus vaccine.
- GeoVax-BravoVax is working to develop a Modified Vaccine Ankara (MVA).

## 15. Symptomatic Drugs

Currently no treatment recommended for Coronavirus infections, therefore, supportive care must be needed. Several antiviral and other agents have been used during Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) outbreaks, but the efficacy of these drugs has not been established. On 18<sup>th</sup> March, 2020, WHO declared that they have started trials of the most promising antimalarial drugs Chloroquine and Hydroxychloroquine, a new antiviral drug Remdesivir and combination of two HIV drugs called Lopinavir and Ritonavir. These HIV drugs are also tested in combination with an antiviral drugs called Interferon beta. The preventive measures are same as for rhinovirus infection such as hand washing and careful disposal of materials infected with nasal secretions. Surface disinfection is also important as it is found that the solid surfaces contaminated with infected material and dried can bear the virus for on days. Disinfection with minimum of 70% of alcohol is quite effective for symptomatic treatment.

## 16. Prevention of Novel Coronavirus Disease (COVID-19)

According to the Public Service Announcement by Ministry of Health and Family Welfare, Govt. of India, we can prevent novel Coronavirus infection by following the ways:

### Do's

1. Wash your hands properly at every 20 to 30 seconds using soap- water or hand wash.
2. Use minimum 60% alcohol-base hand sanitizer.
3. Cover your nose and mouth with triple layered face mask; cloths should be used after proper cloth wash by detergent.
4. Cover your nose and mouth with disposable tissue or flexed elbow when you cough or sneeze.
5. Avoid close contact with people who are unhealthy, make 6.0 feet distance from interaction of people.
6. Stay home, to maintain self-quarantine in the household if you feel unwell.
7. Drink hot water, tea or coffee.
8. Eat some immunity boost up fruits, vegetables etc.

### Don't

1. Touch unwontedly your eyes, nose or mouth when your hands are not clean.

**Prevention is always better Than Cure.....**

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