

A review of widespread viral infection: Human corona virus

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Abstract

The most leading problem that the whole country is facing is the, "CORONA VIRUS". The main purpose of the research is to know the molecular structure and the life cycle of the corona virus. The origin and spread of corona virus is elaborated. The worldwide this viral spread makes it important to know about the clinical symptoms and the diagnosis of the disease. The paper deals with the course of treatment for the disease. It highlights the efforts of the countries worldwide to find a proper treatment for the disease.

Keywords: human corona virus, structural proteins, hydroxychloroquine, covid-19, wuhan, cough, breathlessness

1. Introduction

Corona viruses are a group of enveloped viruses. They are non-segmented and have single stranded positive sense RNA. They affect vertebrates such as pigs and chickens. Apart from that six corona viruses have been known to infect human hosts. This leads to respiratory diseases among

them, severe acute respiratory syndrome corona virus-2 (SARS-CoV2) and Middle East respiratory syndrome coronavirus (MERS-CoV) highly pathogenic corona viruses species that have resulted in regional and global outbreaks. The international committee on taxonomy of viruses has classified corona virus as follows:

Table 1: Classes of Corona as per ICTV

Order	Nidovirales
Family	Coronaviridae
Subfamily	Coronavirinae
The corona virus divided into 4 genera namely	▪ <i>Alphacoronavirus</i>
	▪ <i>Betacoronavirus</i>
	▪ <i>Gammacoronavirus</i>
	▪ <i>Deltacoronavirus</i>

The beta-coronavirus is assigned with four specific lineages namely: A, B, C & D among the six known human corona viruses (HCoVs), HCoV-229E and HCoV-NL63 belong to

Alphacoronavirus, whereas HCoV-OC43 and HCoV-HKU1 belong to lineage A, SARS-CoV to lineage B, and MERS-CoV to lineage C *Betacoronavirus* ^[1].

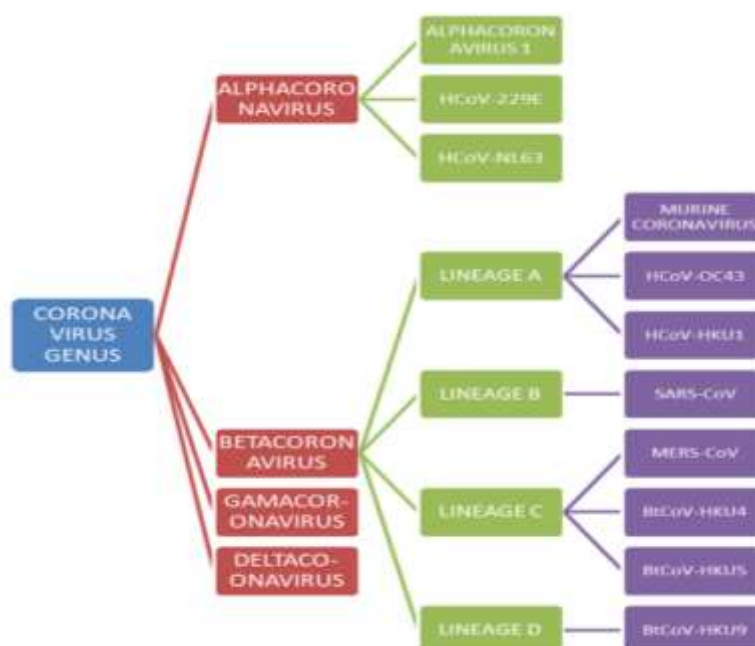


Fig 1: Corona virus genus and their subclasses

2. Molecular Biology of Human Corona Virus

Human corona virus is enveloped and non-segmented. It is approximately 120nm in diameter and is likely to be spherical. It consists of petal shaped projections called as spikes. These spikes are made up of spike protein which is in turn made up of heavily glycosylated type I glycoprotein. A subset of corona virus has an additional layer made up of hemagglutinin-esterase protein (HE), which is termed as short spikes. These short spikes are not important for viral infectivity. The envelope is made up of lipid bilayer and the large and sharp spikes are anchored into the bilayer. The lipid bilayer is formed by the virus budding from intracellular membranes. Other number of elements adhere to the envelope are integral membrane protein (M), small membrane protein (sM) or envelope (E). Inside the envelope is a ribonucleoprotein (RNP) core, which comprises the RNA genome and a single species of nucleocapsid protein N. The corona virus genome is non-segmented, single stranded and positive sense. Its size ranges from 27 to 32kb. The genomic RNA is 5'-topped and 3'-polyadenylated and contains different open understanding edges (ORFs). The invariant quality request is 5' - Replicase-S-E-M-N-3' With various little ORFs (encoding embellishment proteins) dispersed among the basic qualities. The coronavirus replicase is encoded by two huge covering ORFs (ORF1a and ORF1b) involving around 66% of the hereditary succession or genome and is legitimately interpreted from the genomic RNA [2].

3. Structural Proteins

3.1 Spike Glycoprotein (S)

The outermost component of corona virus is the S glycoprotein. Its main function is the attachment of the viral antigen to the host cells. It is also responsible for the fusion of virus envelope with the cell membranes. The host's immune response first attacks the S glycoprotein. The S protein is large in size, ranging from 1160 to 1452 amino acids. Inside a coronavirus animal varieties, arrangement variety is generally shown more by S proteins; the variety of the Spike proteins (S1&S2) grouping most likely gives a specific bit of leeway in insusceptible creatures. There are numerous potential N-connected glycosylation locales. The spike protein has N-terminal sign succession and a film mooring plan close to the C end. The S protein might be cut into S1 and S2 subunits. The cell type determines the extent of S cleavage. This cleavage leads to generation of two major glycopolypeptides as follows: N-terminal S1 and C-terminal S2. S1 and S2 are linked to each other by non-covalent linkage. The breakage can be caused without disrupting the spikes. This is done by the treatment of trypsin of MHV virions. The S1 can be released from the virion by urea or mild alkali treatment. As the whole genome of the corona virus is considered, the S2 is more conserved

than S1. The S2 polypeptide has two areas with seven buildup periodicity which structures wound structure.

The two major role of the Spike (S1 &S2) protein are as follows:

1. It is responsible for the fusion of the virus bilayer with the cellular membranes. This is necessary for viral entry into the cell. S protein is sufficient for the membrane fusion.
2. S protein is responsible for viral binding to the receptors of the target cells [3].

3.2. Integral membrane protein (m)

The M protein is the structural protein essential for the production of corona virus like particles. The M polypeptide is made up of 225-230 amino acids. The amino terminal 20 or so residue of mature M protein of all corona viruses is hydrophilic. They are exposed to the virion surface. They contain small number of glycosylation sites. The remainder of the N-terminal half of the molecules form three helical membrane. The structure of the C-terminal half is not known for sure, yet it is accepted to [3].

3.3. Hemagglutinin-esterase glycoprotein

This is considered to be the mysterious gene. The corona virus belonging to the MHV group possess the HE gene. The product of this gene is not necessary for the viral replication. Not all virus strains express the HE protein [4].

3.4 Small Membrane Protein (E)

It was earlier considered that the corona virus consist of three structural proteins namely S, M, N or four (HE). It is now proved that the virion contains an additional protein called as the small membrane protein which is very essential for the virion assembly. It is clearly known that the E and M protein are very essential for the virion assembly [4].

3.5 Nucleocapsid Protein (N)

The N protein is a 50-60 kilo-Dalton phosphoprotein. This along with the genomic RNA forms a helical nucleocapsid. This is about 9-11 or 14-16nm in diameter. The nucleocapsid protein provides only limited protection to the RNA genome against the various enzymes like ribonucleases. The N protein contains 377 to 455 amino acids. This is highly basic in nature and has high serine content (7-11%) [4].

4. Replication cycle of corona virus

The various steps involved in the replication cycle of the corona virus are as follows:

- 4.1. Attachment and entry
- 4.2. Translation of viral replicase
- 4.3. Genome transcription and replication
- 4.4. Translation of structural proteins
- 4.5. Virion assembly and release

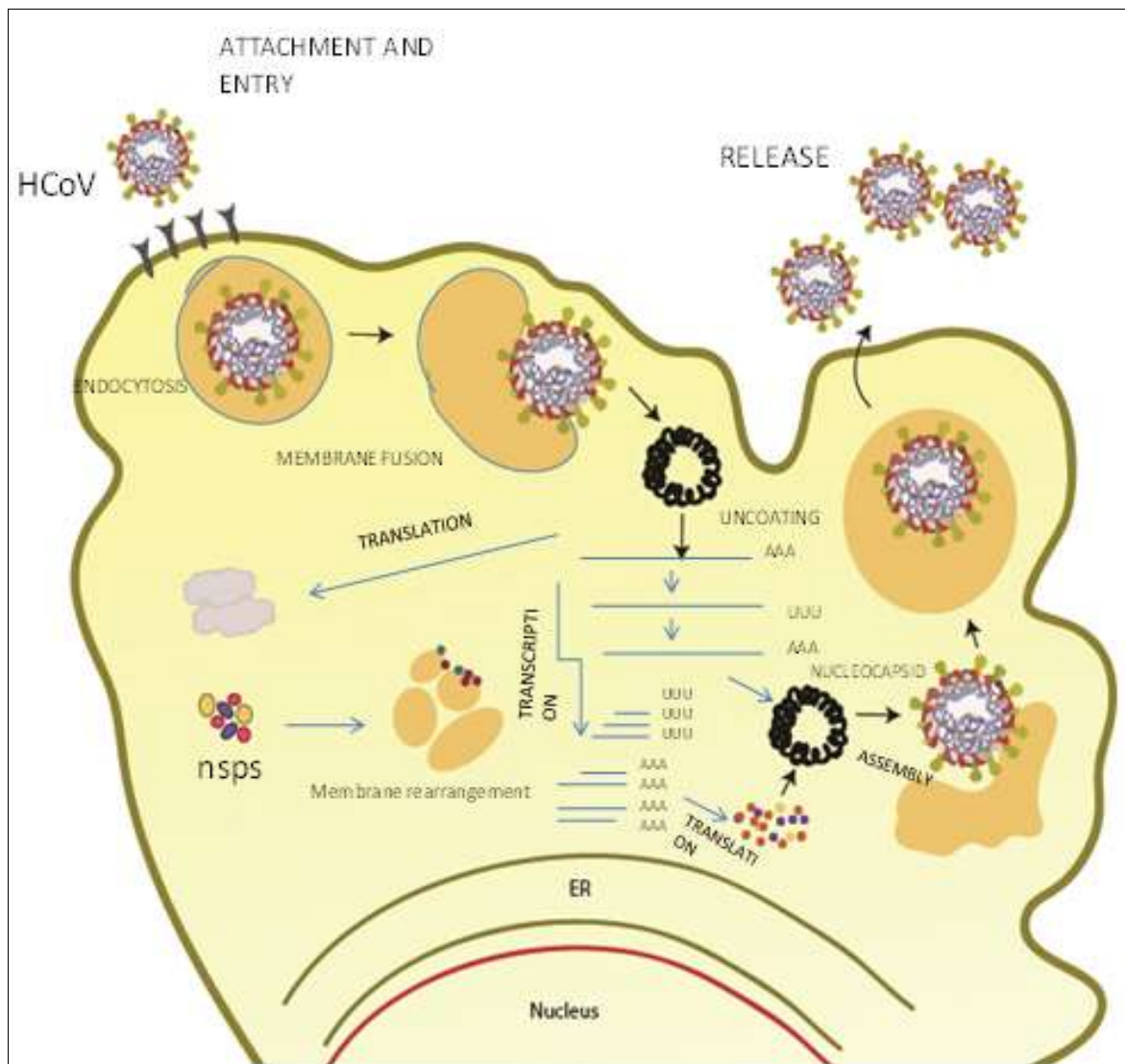


Fig 2: Replication cycle of SARS CoV-2⁵

The first step of coronavirus replication is the binding of S protein to the cell surface receptors. The S protein has two subunits: S1 called as the bulb which is responsible for the receptor binding and S2 called as the stalk responsible for the fusion of the cell membranes. When the S1 binds to the receptor, it triggers a conformational change in the S2 subunit. This in turn results into fusion between the virus envelope and the cellular membrane and release of nucleocapsid in the cytoplasm. Some of the cell surface enzymes like aminopeptidase N (APN) for HCoV-229E, angiotensin converting enzyme 2 (ACE2) for HCoV-NL63 and SARS-CoV, and dipeptidyl peptidase 4 (DPP4) for MERS-CoV are used as receptors by some human coronavirus. One or more host proteases governs the cleavage of S protein into S1 and S2. Host factors could also restrict the attachment and entry of HCoV. For example, interferon-inducible transmembrane proteins (IFITMs) exhibited broad-spectrum antiviral functions against various RNA viruses. The entry of SARS-CoV, MERS-CoV, HCoV-229E, and HCoV-NL63 was restricted by IFITMs^[5].

4.2 Translation of Viral Replicase

After the entry and Uncoating, the RNA serves as a transcript. This leads to cap dependent translation of the open reading frame-1a to produce polyprotein-1a (pp-1a). The slippery sequence and an RNA pseudoknot near the end

of open reading frames-1a enable 25-30% of the ribosome to undergo frame shifting. This produces longer polyprotein which is termed as pp-1ab. The autoproteolytic cleavage of pp1a and pp1ab generates 15–16 nonstructural proteins (nsps) with various functions. The RNA-dependent RNA polymerase activity is encoded in nsp12. The papain like protease and main protease activity is encoded at nsp3 and nsp5. The other non-structural protein starts the rearrangement of cellular membrane to form double membrane vesicles. This leads to the coronavirus replication transcription complex^[6].

4.3. Genome replication and transcription

The genomic RNA is used as a template to synthesize negative-sense antigenome. This is then used as a template to synthesize the new genomic RNA. There are specific sites called the transcription regulated sequences where the polymerase can switch template during discontinuous transcription^[7].

4.4 Virion Assembly and Release

The particle assembly is governed by M protein. This occurs in the ER-Golgi intermediate compartment. The interactions of M protein lead to the virion morphogenesis. The Interaction between the M protein and the S protein as well as M protein and N protein lead to transfer of structural

components to the assembly site. The E protein also contributes to the virion assembly. Finally the coronavirus particles are transported to the smooth wall vesicles and released by exocytosis. You can see in given Figure (fig.2) Whole replication cycle in brief flowchart clipart for reference [8-9].

5. Covid-19 Epidemiology

The new public health crisis threatening the world is the emergence and spread of the novel corona virus. The virus originated in bats and was transmitted to humans through other unknown intermediary animals [10]. This started in Wuhan, China in December 2019. This disease has affected many people worldwide. Till 5th march 2020, there were 96000 reported cases of coronavirus disease and 3300 reported deaths [11]. The transmission of this disease takes place by inhalation or close contact with the infected person. This disease is mild in most cases. If the severity increases it may lead to pneumonia, acute respiratory distress syndrome and multi organ dysfunction. Many people are asymptomatic¹². The fatality rate is estimated to be 2-3%. This disease has had a huge global impact. It is continuing to affect people all over the country [13].

Table 2: The number of cases and death of COVID – 19 outbreaks according to WHO situation reports 20th May, 2020.

Country	Cases	Death	Region
China	4,999,235	325,125	Asia
Singapore	29,364	22	Asia
Hong Kong	1,056	4	Asia
Thailand	3,034	56	Asia
South Korea	11,110	263	Asia
Japan	16,367	768	Asia
Malaysia	6,978	114	Asia
Germany	177,827	8,193	Europe
Australia	7,079	100	Australia
Vietnam	324	00	Australia
United State	1,570,583	93,533	North America
France	180,809	28,022	Europe
Macao	124,603	7,119	Asia
United Kingdom	248,818	35,341	Europe
United Arab emirates	25,063	227	Asia
India	106,886	3,303	Asia

- Updated data of COVID-19 Pandemic in India (20-22 may 2020)

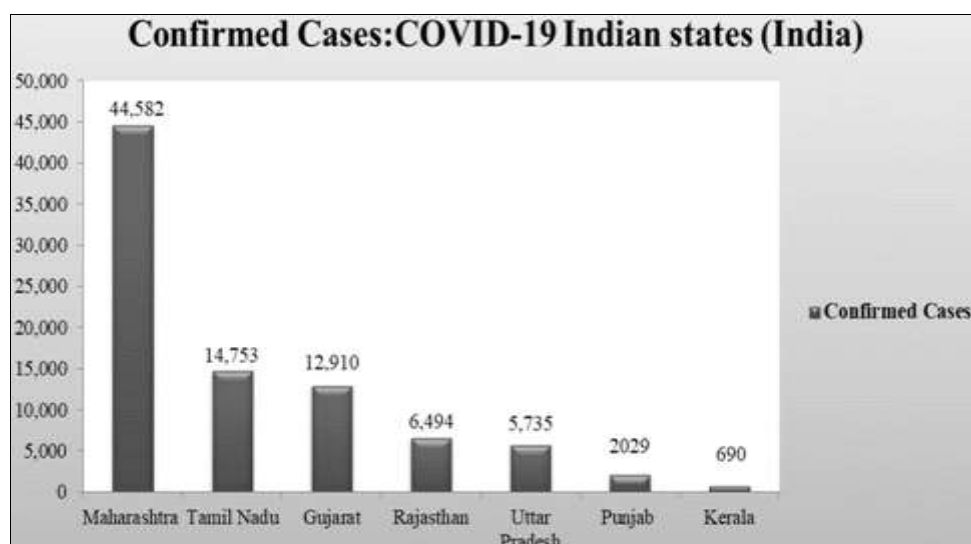


Fig 3: Confirmed Case statistic of COVID-19 in India

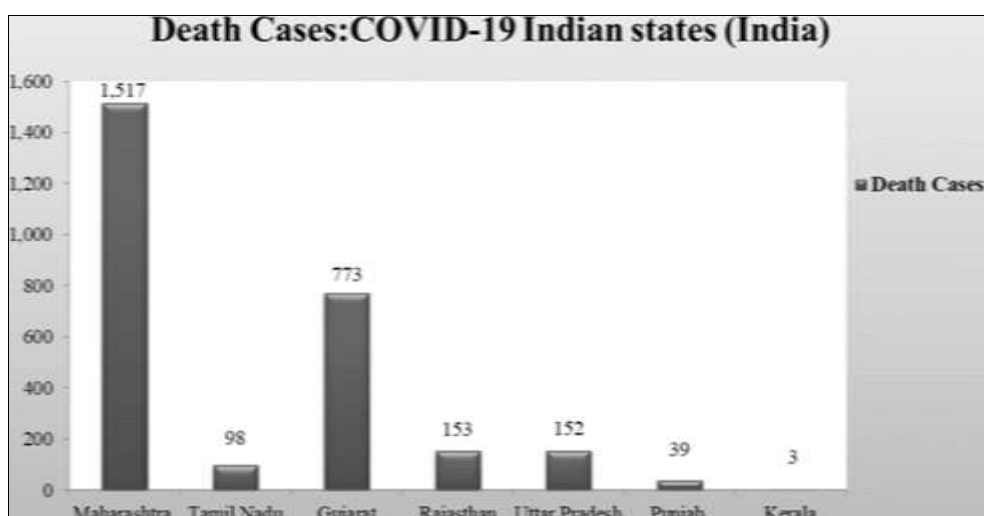


Fig 4: Statistic of Death cases

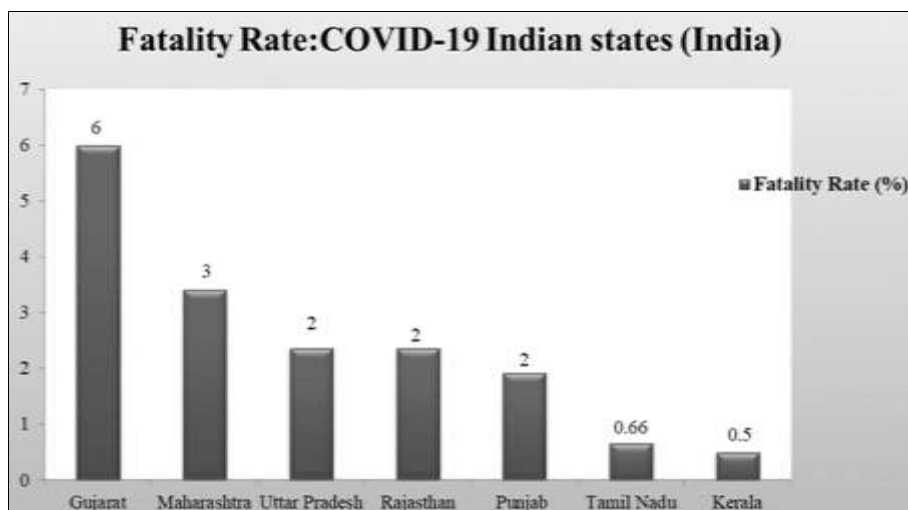


Fig 5: Statistic of fatality rate (COVID-19) in India

Table 3: Statistics of COVI I) 19 ralide MIC 111 Nlatiaraslitra (updated up to 21) may 2020)

District	Number of Cases	Revered cases	Death reported
Mumbai City + Muntiai Subarban	24,118	4,702	841
Thane	4,900	1,103	79
Raigad	532	114	16
Palgbar	475	177	14
Total in metropolitan region	30, 025	6, 096	950
pune	4,477	1,874	226
Aurangabad	1, 082	411	36
Nashik	868	639	36
Solapur	505	156	27
Nagpur	423	269	6
Akola	310	120	17
Jalgaon	303	120	33
Satara	170	95	2
kolhapur	139	11	1
Amravati	123	66	14
Ratnagir	116	32	3
Hingoli	107	86	0
Yavatmal	102	89	0
Dhule	84	47	9
Nanded	80	34	4
Ahmednagar	64	43	5
Sangali	57	33	1
Latur	50	28	2
Jalna	38	8	0
buldhana	34	24	3
Nandurbar	25	20	2
Osmana bad	11	4	0
sindhurg	10	4	0
Parbinsu	9	1	1
Washim	8	1	0
Ilhandara	7	1	0
Gadchiroli	6	0	0
Beed	5	1	0
Chandrapur	5	4	0
%Vanilla	3	o	1
Gondia	1	1	0
Other slates	48	0	11
Total (all districts)	39, 297	10,318	1,390

6. Origin and spread of covid-19

The origin of corona virus disease traced back to Wuhan, Hubei province in China. In December 2019, the adults in Wuhan started complaining about severe pneumonia with an unknown cause. The common findings in most of the initial cases were common exposure to the Humana wholesale sea

food market that also traded live animals [14]. On 31ST December, china reported this to the world health organisation and hence on 1sr January the market was closed down. On 7th January the corona virus was identified. It had similarities with the bat coronavirus and the acute respiratory syndrome corona virus. Environmental samples

from the market were tested positive and this showed the origin of the virus from the market. The first fatal case was reported on 11th January 2020. By 23rd January; the 11 million populace of Wuhan was set under lock down with limitations of section and exit from the area. Before long this lock down was stretched out to different urban areas of Hubei region. Instances of COVID-19 in nations outside China were accounted for in those individuals with no history of movement to China. This demonstrated nearby human-to-human transmission was happening in these nations. Air terminals in various nations incorporating India put in screening systems to distinguish symptomatic individuals coming back from China and set them in seclusion and testing them for COVID-19. Before long it was obvious that the disease could be transmitted from asymptomatic individuals and furthermore before beginning of side effects. Consequently, nations including India who cleared their residents from Wuhan through extraordinary flights or had explorers coming back from China set all individuals symptomatic or in any case in seclusion for 14 days and tried them for the infection. The cases continued to increase exponentially. Although the cases have decreased in China, they have increased exponentially in countries including South Korea, Italy and Iran ^[14].

7. Clinical Symptoms of Covid-19

The manifestations are typically fever, hack, sore throat, shortness of breath, weakness, and discomfort among others. While the incubation time of the infection was at first idea to be 14 days, different cases have been accounted for with shorter courses of events. 43.8% patients had fever while and 67.7% had hack as a typical manifestations. The Chinese Centre for Disease Control and Prevention has detailed that 87% of affirmed cases were in grown-ups matured somewhere in the range of 30 and 79 years. The mortality and case casualty rate expanded with expanding ages; the case casualty rate was 8% in patients matured somewhere in the range of 70 and 79 years while it was 15% in those matured 80 years or more. The basic clinical highlights incorporate fever (not on the whole), hack, sore throat, cerebral pain, exhaustion, migraine, myalgia and shortness of breath. Conjunctivitis has additionally been portrayed. The study also reported that the patients had prolonged virus shedding in the respiratory tract and faeces ^[15].

8. Testing for covid-19

A suspect case is defined as the one with fever, sore throat, and cough. They may have a travel history to china or any other areas where this disease is spreading. There may be some contact with patients suffering from the disease. A suspect may be asymptomatic or without fever. Different molecular tests are carried out. Specific molecular tests are done on respiratory samples like throat swab, sputum, nasopharyngeal swab, etc. The presence of virus may be in the stool in some cases. In serious cases blood samples may also contain the virus. There are no commercial cases available at present. But as the disease progresses, commercial tests will be available. In India, the samples are taken and are tested in designated reference labs or the national institute of virology in Pune. The white cell count is usually low in such cases. The platelet count is usually normal or mildly low. The C-reactive protein and erythrocyte sedimentation rates are generally elevated¹⁶. The

procalcitonin levels are generally normal. The ALT/AST, prothrombin time, creatinine, D-dimer, CPK and LDH may be elevated and high levels are associated with severe disease. The chest x-rays are normal in early disease but as the disease progresses it may show bilateral infiltrates. The CT is more helpful as it is more specific. The CT is also useful to detect the disease in asymptomatic patients. CT has been used to detect the disease in patients which showed negative molecular diagnosis ^[17].

9. Treatment for Covid-19

The very first step to treatment is isolation. Isolation should be done to prevent transmission to other people like the healthcare workers. Mild illness can be managed at home. Hydration and nutrition are the factors which should be controlled ^[15]. Mild fever and cough can be maintained at home. Routine utilization of anti-infection agents and antivirals, for example, oseltamivir ought to be stayed away from in affirmed cases. In hypoxic patients, provision of oxygen through nasal prongs, face mask, high flow nasal cannula (HFNC) or non-invasive ventilation is provided. Mechanical ventilation may also be used. Renal replacement may be needed in some cases. Low to moderate doses of corticosteroids are also recommended. Antiviral medications, for example, ribavirin, lopinavir ritonavir have been utilized dependent on the involvement in SARS and MERS. In an authentic control concentrate in patients with SARS, patients treated with lopinavir-ritonavir with ribavirin would do well to results when contrasted with those given ribavirin alone. In recent times Hydroxychloroquine is recommended on large scales along with the drugs used for treating HIV ^[16, 17].

10. Clinical trials for treatment of Covid-19

Europe has started clinical preliminaries of trial medications to treat COVID-19 out of thousands of patients including a much discussed antimalarial sedate, chloroquine. The preliminaries will remember the fundamentals will recollect 3,200 patients for the Netherlands, Belgium, Luxembourg, the United Kingdom, France, and Spain. There will be 800 patients in France, where clinical fundamentals were impelled this past week's end. The drug trials include antiviral drugs Remdesivir (used to treat Ebola), Lopinavir/Ritonavir (used to treat HIV/AIDS) and hydroxychloroquine (used to treat malaria). The drug had been used to treat 24 people in Marseille with COVID-19 at a university hospital institute and the preliminary results of that trial were published on March 20 in the International Journal of Antimicrobial Agents. The study concluded that despite the small sample size, the treatment with a type of chloroquine (hydroxychloroquine) and an antibiotic showed a "reduction/disappearance" of the virus in several patients. "Following six days, there was an extremely noteworthy contrast between the individuals who were dealt with as opposed to not-treated," said irresistible ailment master Didier Raoult who runs the establishment in Marseille where the little preliminary was completed. He said 75% of the patients improved with the treatment ^[17, 18].

11. Prevention of Covid-19?

The CDC prescribes different strides to forestall the transmission and danger of SARS-CoV-2. Visit hand washing enduring in any event 20 seconds by utilizing cleanser and water is exhorted. Hand sanitizers with any

rate 60% liquor can likewise be utilized as another option. The general population has likewise been advised to abstain from contacting mucosal surfaces, for example, the mouth and the nose with hands that have not been washed. Anybody indicating manifestations of the infection should attempt to look for suitable clinical assistance. They ought as far as possible their introduction to other unaffected individuals and spread their noses and mouths when hacking or wheezing. They are likewise encouraged to wear a facemask on the off chance that they present with side effects. Visit cleansing and cleaning are prompted for bunches that are at danger of getting the infection ^[19].

12. Conclusion

The corona virus disease is spreading at an alarming rate. The easiest way to control it is to maintain social distancing and by improving innate immunity. The treatment given is being updated as the results of clinical trials are coming up. The virus though microscopic is causing much harm to the public health. The origin and its spread help us to have a better view at the disease that has been affecting the whole human race worldwide.

Table 4: List of Abbreviations

SARS	Sever Acute Respiratory Syndrome
CoV2	Corona virus2
MERS	Middle East Respiratory syndrome
HCoV	Human Corona Virus
HE	Hemagglutinin Estrase
RNP	Ribonucleoprotein
M	Membrane protein
SM	Small membrane protein
E	Envelop
N	Nucleocapsid
ORF	Open reading Fame
RNA	Ribonucleic acid
MHV	Mouse Hepatitis Virus
S1	Spike 1
S2	Spike 2
ACE2	Angiotensin Converting Enzyme 2
DPP4	Dipeptidyl Peptidase
IFITMs	Interferon induced Transmembrane Proteins
PP-1a	Polyprotein-1a
NSPS	Non-structural proteins

13. Declaration of Competing Interest

The authors report no conflict of interest in this work

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