Review Article

COVID-19 Outbreaks: Global Pandemic Disaster (An Overview)

Gulzar Alam*, Jai Narayan Mishra, D K Vishwakarma, Abhay Pratap Singh, Amit Rai, Amit Kumar Shukla, Wajahat Ullah Khan, Amrendra Singh, Satendra Mishra

[a] Kailash Institute of Pharmacy & Management, GIDA, Gorakhpur, Uttar Pradesh, India.

***Corresponding author's E-mail:** gulzar_alam@rediffmail.com

Received: 25-03-2020; **Revised:** 22-05-2020; **Accepted:** 30-05-2020.

ABSTRACT

First step of corona virus in Wuhan, a city of China, in December 2019, spread throughout the world and becoming a global health emergency announced by World Health Organization and named as. ssRNA virus is highly infective and spread as through coughing or sneezing. By this time (23 April, 2020) more than 200 countries 175694 deaths are claim. The most common symptoms of COVID-19 are fever (99%), fatigue (70%), dry cough (60%), myalgia (44%) and dyspnoea. The clinical features of COVID-19 are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction. Several existing antiviral agents are being used under clinical trial. Only supportive therapy is the treatment strategy followed by health professionals. Supportive therapy includes administration of antipyretic and analgesic, maintenance of hydration, mechanical ventilation as respiratory support and uses of antibiotic in bacterial infections. In India, the status of COVID-19 is pathetic but strategically under control. Social distancing, proper hand hygiene and follows the instruction of Government of India, are helpful in spreading and controlling COVID-19.

Keywords: COVID-19, Respiratory droplets, Supportive therapy, Social distancing, Hand hygiene.

INTRODUCTION

Due to its "crown" like appearance, this novel virus named corona. Although in 1968, the word "corona virus" was come first time into the people.[1] Corona virus established itself in the world in 2003 in the form of severe acute respiratory syndrome (SARS) and in 2012 as Middle-East respiratory syndrome corona virus (MERS CoV). Corona viruses (CoVs) representing a major group, mostly affecting human beings through zoonotic transmission.[2,3] In current time, the first infected person from corona virus was reported in Wuhan, China, in December 2019 and this virus named as novel coronavirus (2019-nCoV). From china it is continuously spread through the globe. The spreading of corona virus leads dangerous to human beings so that the World Health Organization (WHO) declares it as global health emergency and give the name of disease cause by this virus as COVID-19, which means coronavirus disease 2019. COVID-19 is also known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or SARS-related CoV-2.[4,5]

TAXONOMY OF CORONA VIRUSES

As per International Committee on Taxonomy of Viruses, corona viruses are classified as:

Order: Nidovirales,

Family: Coronaviridae

Sub-family: Coronavirinae

Due to difference in genomic structure corona viruses are divided into four categories viz; α-corona virus, β-corona virus, γ-corona virus and δ-corona virus. All six know human corona virus belongs to beta category. Four distinct lineages (A, B, C, and D) have been assigned within the genus β-corona virus. Among the six known human coronaviruses (HCoVs), HCoV-229E and HCoV-NL63 belong to α-corona virus, whereas HCoV-OC43 and HCoV-HKU1 belong to lineage A, SARS-CoV to lineage B, and MERS-CoV to lineage C β-corona virus.[6,7]

STUDY OF CORONA VIRUS-PATHOGENESIS

The genomic sequences of corona viruses are most studied genome among all RNA containing virus. 2/3rd portions of genome exhibit viral polymerase and RNA synthesis genes while 1/3rd containing genomic sequences for four specific proteins includes spike (S), envelope (E), membrane (M) and nucleocapsid (N) (Figure 1 and 2). Spike protein is responsible for entry into the host cell. Further expression of genes takes place inside the human cells and provide suitable environment for multiplication of virus.[8,9]

SARS-CoV enters into the host cells by binding with angiotensin-converting enzyme-II cellular receptor. Once the virus enters into host cells its reside in cytoplasm where its RNA synthesizes various protein which help in replication of genetic materials and of course its multiplication. After duplications the buds of virions are present into the lumen of the endoplasmic reticulum. Exocytosis process helps in the release of these virions. Virions are then released from the infected cell through exocytosis. These newly produced virions infected vital organs of human such as kidney, liver, lower respiratory tract etc.[10] This virus can make the antiviral T-cell response irregular due to the stimulation of T-cell apoptosis, thus causing a collapse of the immune system.[11,12]

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

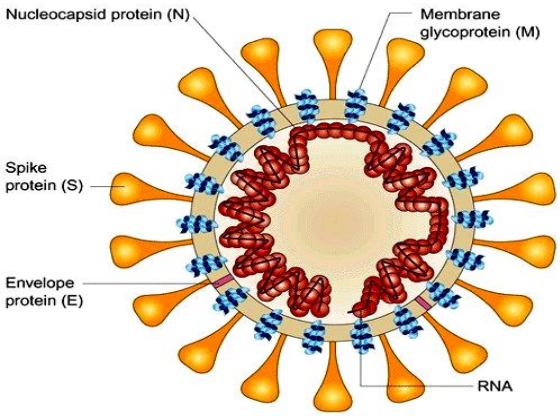

Figure 1: Diagrammatic representation of corona virus[13]

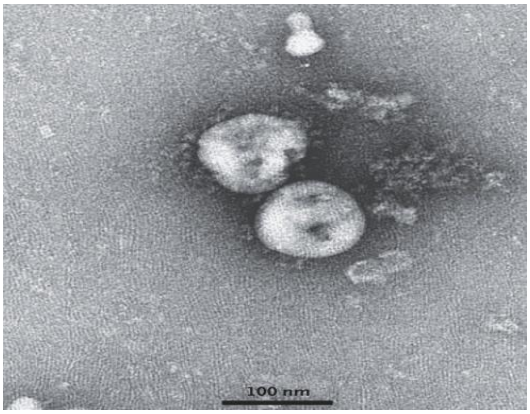

Figure 2: Transmission Electron micrograph of the COVID-19[13]

Transmission

The initial cases were presumably linked to direct exposure to infected animals (animal-to-human transmission) at a seafood market in Wuhan, China. However, clinical cases with diversity in exposure history have emerged. This helps further elaborate that human-to-human transmission of the virus is also possible. Therefore, human-to-human transmission is now considered the main form of transmission. Individuals who remain asymptomatic could also transmit the virus. However, the most common source of infection is symptomatic people. Transmission occurs from the spread of respiratory droplets through coughing or sneezing. Data also suggest that close contact between individuals can also result in transmission. This also indicates possible transmission in closed spaces due to elevated aerosol concentrations. SARS-CoV-2 has a basic reproduction number of 2.2. This suggests that a patient can transmit the infection to two other individuals. Current data suggest that the virus has an incubation period of three to seven days.[20]

However, more advanced virological and genetic studies have shown that bats are reservoir hosts of both SARS-CoV and MERS-CoV and before these viruses spread to humans, they use the other responsible animals as intermediate hosts. Studies have reported that most of the bat corona viruses are the gene source of alpha- corona viruse and beta- corona viruses, while most of the bird corona viruses are the gene source of gamma- corona viruses and delta-corona viruses.[14] In recent studies, it has been observed that the novel virus causing epidemics coincides with the corona viruse isolated in bats. Presence of wild animal trade in Huanan Seafoods Market where the first cases appeared, supports this finding.[15] The first non-Chinese case of the infection, which spread to the Chinese provinces, and then to the Asian continent, was reported from Thailand on January 13, 2020. The case reported being a Chinese tourist who has traveled to Thailand and had no epidemiologic connection with the marketplace.[16] Other cases from oversea countries such as the USA and France have continued to be reported.[17] Often, the human-to-human transmission occurs with close contact. The transmission primarily occurs when an infected person sneezes and through the respiratory droplets produced just as the spread of influenza and other respiratory pathogens. These droplets can settle in the mouth or nasal mucosa and lungs of people with inhaled air. Currently, it remains unclear whether a person can be infected by COVID-19 by touching an infected surface or object and then touching their mouth, nose or possibly eyes (Figure 3).[18]

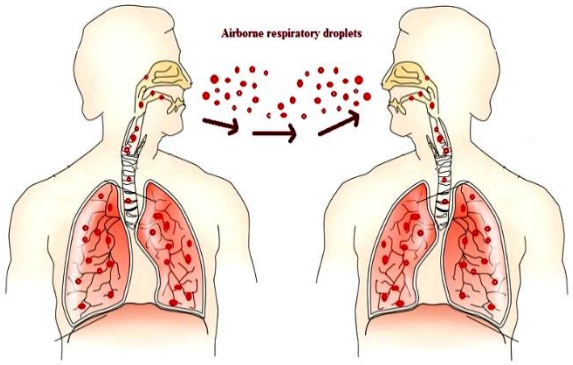

Figure 3: Transmission of corona virus via airborne droplets

Epidemiology and Spread of COVID-19

On 31 December 2019, China was reported to WHO about disease which shows pneumonia like symptoms. Meanwhile on January 2020, scientist from China declares the emergence of new virus and named it as 2019-nCoV.[19] On 11th January 2020, first death was reported in China. After declaration of this viral disease, patients infected from this virus increases exponentially. The healthcare professionals who look after infected persons also get suffered which confirms human to human transmission of this virus.

Seeing the severity of infection and epidemic doubling rates i.e. 1.8 days, lock down was placed in Wuhan on 23rd January.[20] As on 28th February, 2020, there have been 83,704 confirmed cases of COVID-19 globally, with 2,859 deaths. Most cases have been reported from mainland China.[21] As on 5th March 2020, 96,000 cases worldwide

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

(80,000 in China) and 87 other countries and 1 international conveyance (696, in the cruise ship Diamond Princess parked off the coast of Japan) have been reported.[22]

Upto 3rd March 2020, there was only 3 active case of COVID-19 were reported in India and sudden increase in cases were observed. 29 cases were reported from different city of India viz. Delhi, Agra and Jaipur in Italian tourists and their contacts, by 5th March 2020. An Indian passenger, who comes bake his home and celebrate birthday party with a number of people, was found to be corona. The patient and all contacts of these cases have been quarantined.

The current situation from suffering of COVID-19 is very serious throughout the world (Figure 4 and 5, Table 1). In India, the condition is still under control but spreading of COVID-19 is continues (Table 2).

Table 1: Laboratory-confirmed COVID-19 cases and deaths. Data as of 14 May 2020 (Major countries).[23]

Reporting Country	Total confirmed cases	Total confirmed new cases	Total deaths
China	84464	6	4644
Spain	228691	661	27104
Italy	222104	888	33106
Germany	172239	933	7723
The United Kingdom	229709	3242	33186
France	138609	448	27029
Belgium	252245	9974	2305
Iran (Islamic Republic of)	112725	1958	6 783
United States of America	1340098	18044	80695
India	**78003**	**3722**	**2549**
Globally	**4248389**	**77965**	**294046**

Table 2: India COVID-19 cases by state/UT. Data as of 14 May 2020.[24]

Name of State / UT	Confirmed	Cured Cases	Death
Andaman and Nicobar Islands	33	33	0
Andhra Pradesh	2137	1142	47
Arunachal Pradesh	1	1	0
Assam	80	39	2
Bihar	940	388	7
Chandigarh	187	28	3
Chhattisgarh	59	55	0
Delhi	7998	2858	106
Goa	7	7	0
Gujarat	9267	3562	566
Haryana	793	418	11
Himachal Pradesh	66	39	2
Jammu and Kashmir	971	466	11
Jharkhand	173	79	3
Karnataka	959	451	33
Kerala	534	490	4
Ladakh	43	22	0
Madhya Pradesh	4273	2004	232
Maharashtra	25922	5547	975
Manipur	2	2	0
Meghalaya	13	10	1
Mizoram	1	1	0
Odisha	558	143	3
Puducherry	13	9	1
Punjab	1924	200	32
Rajasthan	4328	2459	121
Tamil Nadu	9227	2176	64
Telangana	1367	940	34
Tripura	155	16	0
Uttarakhand	72	46	1
Uttar Pradesh	3729	1902	83
West Bengal	2290	702	207
Total	**78003**	**26234**	**2549**

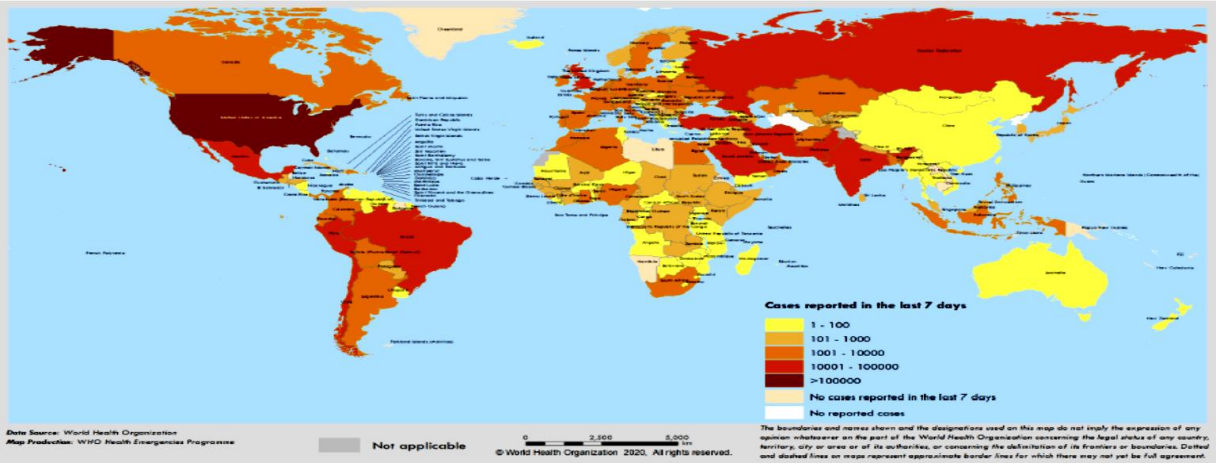

Figure 4: Globally reported confirmed cases of COVID-19 in last seven days, 14 May 2020.[23]

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

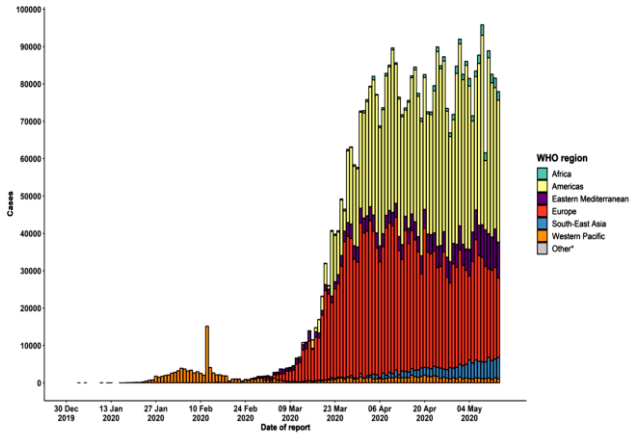

Figure 5 Graphical presentation of confirmed COVID-19, on 14 May 2020.[23]

CLINICAL MANIFESTATIONS AND DIAGNOSIS

The most common symptoms at illness onset are fever (99%), fatigue (70%), dry cough (60%), myalgia (44%) and dyspnoea. Less common symptoms are headache, dizziness, diarrhoea, nausea and vomiting. Symptoms such as pharyngeal pain, dyspnoea, dizziness, abdominal pain and anorexia are more likely to be present in patients with severe illnesses.[25] Based on the severity and symptoms of the patients, the COVID-19 may be classified into following categories.[26]

a. Mild stage symptoms

Patients who has upper respiratory tract viral infection, shows symptoms like congestion in nasal tract, dry coughing, malaise, sore throat and sore throat. Serious symptom i.e. breathing difficulties is generally absent in mild stage. About 81% cases of COVID-19 shows mild severity but if proper treatment and management of virus not given at this stage then this mild stage may change into severe to critical stage.

b. *Moderate stage symptoms*

The respiratory symptoms like dyspnea, tachypnea and coughing are the more common at moderate infection. Severities of symptoms are less common.

c. Severe stage symptoms

Patients with severe disease present with severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis or septic shock. Even in severe forms of the disease, fever can be absent or moderate. Patients with pre-existing comorbidities have a higher case fatality rate. These comorbidities include diabetes (7.3%), respiratory disease (6.5%), cardiovascular disease (10.5%), hypertension (6%), and oncological complications (5.6%). Patients without comorbidities have a lower case fatality rate (0.9%).

The initial stage symptoms are very common and similar to others influenza, distinction of the symptoms of corona virus quite difficult. The symptoms like fatigue, cough, headache, myalgia, sore throat and breathlessness are more common.

As the disease progresses initial phase pneumonia leads to severe respiratory disorders leads to death. As the infection progress, the amount of inflammatory mediators (IL2, IL7, IL10, IP10, MCP1 and TNF-α) rise at extreme levels. In between time patient suffers from dyspnea (within 5 days), hospitalize (7 days) and ARDS (8 days). Critical stage patients (approx. 25-30%) were observed in intensive care unit (ICU). Complicated symptoms like infection in lungs, ARDS and kidney infection was progress. Patients were recovering from diseases after 14-21 days as per severity. Mortality rate was highest (50-75%) in old age patients with pre-comorbidities history while adult patients with high immunity showed fatality rate 4-11%. WHO recommends procedures for testing and collection of sample from the infected patients. Samples for testing can be collected from both the upper and lower respiratory tracts. The collected samples are then tested via RT-PCR (polymerase chain reaction). WHO recommends procedures for testing and collection of sample from the infected patients. Samples for testing can be collected from both the upper and lower respiratory tracts. The collected samples are then tested via RT-PCR (polymerase chain reaction).[29]

CLINICAL MANAGEMENT

At present, there is no vaccine and drugs available to treat this infection. Previously discovered antiviral drugs are used as precautionary measure. Several clinical trials are going on these antiviral drugs. But as per WHO declaration, the discovery of COVID-19 vaccine or drugs will take atleast eighteen month to come in the market.[30]

A case report (South Korea) suggest that the combination of Lopinavir / Ritonavir (the drugs used to treat HIV), interferon and ribavirin showed viral clearance from infected patients. In America, remdesivir was successfully used to treat this infection. Remdesivir, is an antiviral drugs, killed the virus by inhibiting RNA transcription in virus at initial phase.[31] Remdesivir has a strong antiviral activity in epithelial cell cultures against SARS-CoV, MERS-CoV and related zoonotic bat corona viruses.[32]

Lopinavir-ritonavir is FDA-approved for treatment of HIV infection. As it targets protease, it has been used for other coronavirus infections; (used empirically for SARS) and is being studied in the treatment of MERS-CoV.[33] In China, this combination in conjunction with Interferon alpha (IFN-α, an immunomodulatory drug used for hepatitis B & C) is used for treatment of some patients with COVID-19.[34]

Medical guideline of China also recommend moderate dose of corticosteroids as short term therapy in COVID-19.[35] But current research showed that corticosteroid short term therapy did effective.[36] Baricitinib trilas for reduction of virus invasion and inflammation associated with disease. Spike proteins of novel corona virus are the major target site for killing of virus.[37] There are multiple research teams trying to investigate a possible vaccine for the virus. The role of the spike protein in the viral infectivity and pathogenesis is a possible preventive target.[38]

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

For this, several i*n vitro* evaluations of marketed antiviral drugs like nitazoxanide, chloroquine, ribavirin, penciclovir, nafamostat, remdesivir and favipiravir were going on. The results showed that remdesivir and chloroquine are more effective as compared to the others. In America, remdesivir treated patient was reported to have recovered.

Table 3: On-going clinical trials on COVID-19

Clinical trials	Clinical trials No.	Drug's name
Phase III trials	NCT04252664 and NCT04257656	Remdesivir
Open-label trial	ChiCTR2000029609	Chloroquine
Randomized clinical trials	ChiCTRChiCTR2000029544 and ChiCTR2000029600	Favipiravir
Randomized clinical trials	ChiCTR2000029387	Ribavirin with pegylated IFN

There is no special vaccine for this yet. Under this condition, where there is no drugs to treat COVID 19, only supportive therapy is effective strategy adopted by health professionals to combat the situation. The use of NSAID'S, ventilators, proper reparatory support, oxygen therapy and existing potent antimicrobial/ antivirals drugs together constitutes supportive therapy. Patients admitted in ICU are treated with glucocorticoid therapy and plasma therapy with regular supply of high oxygen flow. High-flow nasal oxygen or non-invasive ventilation was providing to patients with respiratory failure. Artificial organs support systems are required for those patients suffer from multiple organ dysfunctions.[41,42]

PREVENTION OF TRANSMISSION

COVID-19 spreads through respiratory droplets and physical contact of infected persons. The viral transmission can be prevented by taking some precautionary measures. WHO recommended some precautionary measures which includes hand hygiene (washing of hand with soap at regular interval), wearing of personal protective equipment (PPE) during handling of COVID-19 patients, wearing of mask and develop cough etiquettes. Hand sanitizers which containing 60-80% alcohol are effective to killed all virus with 20-30 seconds. Hand washing following the correct steps with soap and water should suffice. Cloth towels should be avoided for drying hands and disposable tissue papers should be preferred. PPE consists of the medical masks or particulate respirators, face shields or goggles, gowns, gloves and shoe covers. Particulate respirators (N-95 mouth mask) should be used by health care workers involved in aerosol-generating procedures (AGPs). Face shields/goggles are to be used by all by health care workers while performing AGPs. Long-sleeved, sterile, waterproof gowns, made of non-absorbable materials are to be worn.[43,44]

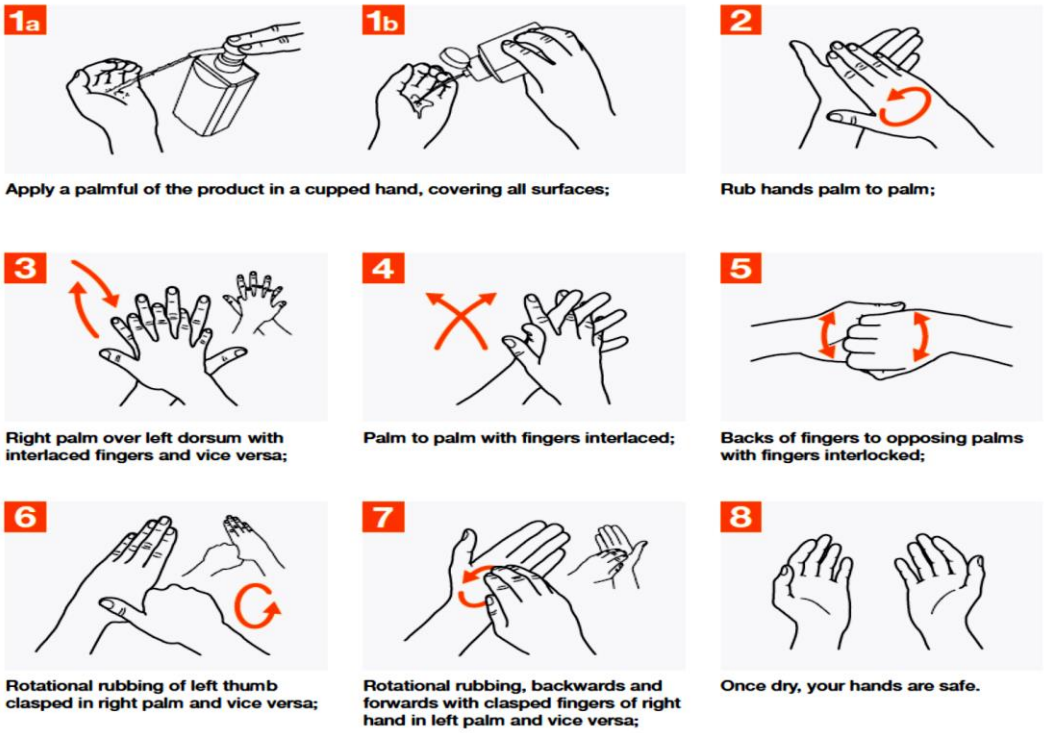

Figure 6: Hand hygiene: Rub hands when hand are visibly soiled[45]

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

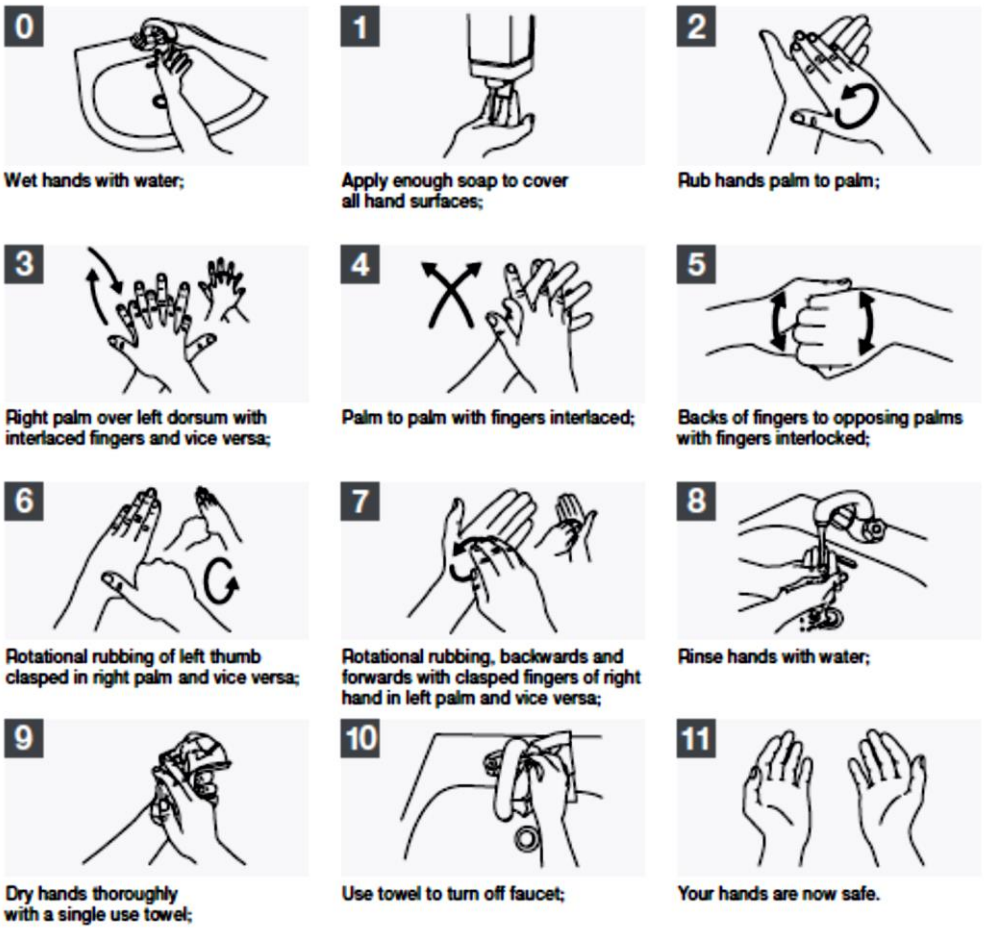

Figure 7: Hand hygiene: Wash hands when hand are visibly soiled[45]

QUARANTINE

According to WHO, "The International Health Regulations (IHR) are an international legal instrument that is binding on 194 countries across the globe, including all the Member States of WHO. Their aim is to help the international community prevent and respond to acute public health risks that have the potential to cross borders and threaten people worldwide". The IHR defines "the rights and obligations of countries to report public health events and establish a number of procedures that WHO must follow in its work to uphold global public health security".[46] In line with the principles outlined in IHR, the Ministry of Health and Family Welfare, Government of India, has issued travel advisories from time to time, looking after the seriousness of this viral transmission. The travel advisory states, "Indian travellers are hereby advised to refrain from travelling to China. After this advisory all existing visas for any foreign national travelling from China become invalid. So the people travelling back to India from China must undergone quarantined.[47]

More than 3700 passenger of a cruise ship docked off Yokohama (Japan) was quarantined for two weeks.[48] On January 23, 2020, China government imposed a lockdown on Wuhan to quarantine and prevents the spread of the disease. This was a drastic public health measure. While the benefits of such a move remain to be seen, the long-lasting negative impacts of such a measure should not be underplayed.[49,50]

PRECAUTIONS

- **Regular washing of your hands:** Frequent washing of hand with soap and water or used alcohol-based hand rub for disinfect your hands (Fig. 6 and 7).
- **Social distancing should be maintained:** A physical distance (approx. 1 meter or 3 feet) must be maintained between yourself and others.
- **Regular touching of nose, mouth and eyes must be avoided:** From contaminated hand the virus can easily entered into the body by touching moth or nose and eyes. So avoid touching of nose, mouth and eyes when come from outside.
- **Develop respiratory etiquette:** During sneezing and coughing one should bent elbow or use tissue paper. Make a habit to wear mask in a crowed area.
- **Must inform if any symptoms and follows advice of your doctor:** If you see any symptoms in yourself or any person, immediately informed your nearby health care center and must follows the advice give by health professional.

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

COVID-19 IN INDIA: HOW TO COMBAT

In India, the first COVID-19 case was reported in Trissur, Kerala, on January 30, 20205. Current evidence suggests that the incubation period may last for 1-14 days, with a mean duration of 5-7 days. The rapid spread of infection is augmented by the potential for transmission by asymptomatic or minimally symptomatic patients.[51] Until now, our national strategy in tackling the COVID-19 has been predominantly one of containment, an approach typically utilized when a pathogen has slow transmission capacity or is brought in from external sources. This allows for the implementation of measures to limit its spread such as quarantine of individuals coming from a high transmission area, isolation of infected individuals, contact tracing as well as reducing the movement of people in areas that have a high case load. The containment strategies adopted by Kerala have helped in slowing the spread of infection into the community by the end of March.[52] However, once the infection starts to spread in the community with evidence of sustained local transmission, it becomes impossible to isolate all the infected individuals. In such situations, mitigation measures are needed with the aim to slow down the spread of infection. These procedures include closure of schools and a ban on public mass gatherings.[53] With the escalating number of COVID-19 cases being detected in our country over the last few weeks, it is time for India to shift its efforts to slow the spread of the SARS-CoV-2 virus from containment to community mitigation.

The community mitigation strategies are called 'flattening the curve' in epidemiological terms. The curve refers to the projected number of people who will contract COVID-19 over a given time frame. The shape of the curve varies according to the rapidity with which the infection spreads in the community. Infection curves with a steep rise also have a steep fall. This results in an overloading of the local healthcare systems beyond their capacity, leading to higher case fatality rates. The highest priority at this stage is to keep the mortality as low as possible.

As the disease spreads in the community beyond the primary contacts, strategies to prevent further spread within communities is the need of the hour. Thus by adopting the below mentioned programme to combat the current situation.

Social distancing

Social distancing measures include isolation of infected people, quarantine of their contacts, options for people to work from home, the closure of schools and the cancellation of large gatherings. Such measures allow our healthcare system to handle the additional burden in a phased manner. The WHO recommends a minimum distance of at least 1 m (3 feet) to be maintained between individuals to prevent the spread of the infection through respiratory droplets. Timely implementation of aggressive strategies that create social distance and reduce close contact of people has proven effective in delaying the rates of transmission and reducing severe illness and death in times of pandemic.[54]

Personal protection measures

Individual protection measures towards the infection control can be achieved by personal commitment and action and at the same time follows the guidelines given by government. Make a habit of regular hand washing or sanitization may reduce the risk of infection. Individuals are encouraged to practice respiratory hygiene. In case a person develops respiratory symptoms, using a medical mask is recommended. External surface which come in touch very frequently should be disinfected at regular basis.[55,56]

Home isolation when sick

The patients with asymptomatic symptoms must be kept at home quarantine for fourteen days. Patients can be managed symptomatically with oral paracetamol. Such patients must be quarantine in single isolated and ventilated room with limited movement. House member should not be entered in quarantine room. A member of family is appointed for take care of him with proper cautions. Every persons who come closed the infected person are suspected and 14 day quarantine period in necessary for them.[57]

Care of the vulnerable population

A critical facet of COVID-19 has been the disproportionately higher mortality seen among individuals more than 60 yr than the young adults or pediatrics population. Those above 80 yr were noted to have the highest case fatality rate at 14.8 percent. An analysis was performed in China including a pool of 72314 patients. The results showed that there were about 44672 confirmed cases, 16186 suspected cases, 10567 clinically diagnosed cases and 889 asymptomatic cases while patients with no prior comorbid conditions had a case fatality rate of 0.9%. The mortality rate was higher in cardiovascular patients about 10.5%, diabetic patients about 7.3%, hypertensive patient about 6% [58]. These findings make it imperative to protect individuals belonging to these highly susceptible groups more strongly. As children may often be asymptomatic transmitters of the disease, their interaction with elderly should be limited.[59]

Widening the testing and treatment capacity

At the start, only government laboratories under the guidance with Indian Council of Medical Research (ICMR) were performing the COVID-19 test by reverse transcription-polymerase chain reaction (RT-PCR) for only those whose international travelling history and his close contact.[60] As the number of patients increases in India, test laboratory and facilities for COVID-19 has scaled up. The ICMR, Pune, successfully confirmed the homology (99.98%) of Indian strain of corona virus with strain from Wuhan. A comprehensive approach is needed to break the chains of transmission, and more aggressive testing; early diagnosis and isolation along with adequate treatment seem to be

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

the way forward in tackling this infection in the future.[61] As India prepares for a worst case scenario, it is of utmost importance for all its citizens to follow strict hygiene practices to ensure self-protection and prevent the further spread of the infection within the community. With these measures, we can hope to tide over the pandemic as early as possible.

Table 4: Summary of test results as per ICMR[62]

Samples tested	500,542
Tests per 1 million people	370
Tested individuals	485,172
Tested positive	21,797

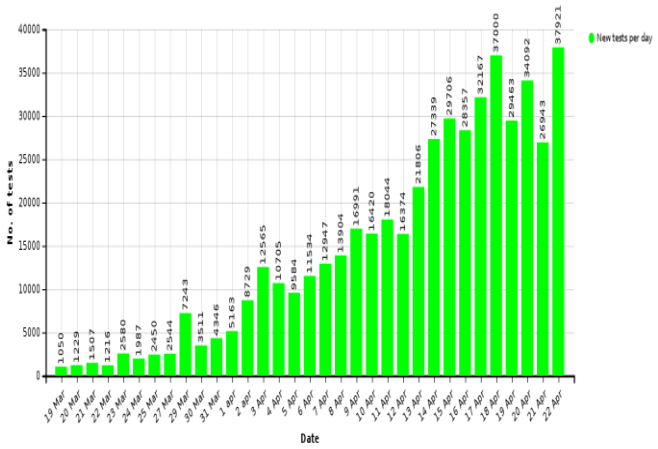

Figure 8: Daily test result summary by ICMR[62]

CONCLUSIONS

In December 2019, patient suffering from pneumonia like symptom has novel corona virus in China (Wuhan). From China this virus spread throughout world and become global health emergency. In February 2020, WHO declares it as COVID-19 (Coronavirus disease 2019). The COVID-19 pandemic challenged whole the world for their economic, medical and public health infrastructure. The extraordinary spreading of COVID-19 brings an alarming stage in front of the whole world. The death and infection rate is so high as compared with SARS or MERS. The three clinical stages are observed start from mild fever with upper respiratory tract infection followed by severe life-threatening pneumonia and finally ends with severe pneumonia (ARDS). Elderly and immune-compromised patients are more prone to get infected since no vaccines and drugs for this virus, some supporting strategies are adopting to take over this situation. Transmission can be controlled by proper hand hygiene, frequent touching of eyes, nose and mouth should be avoided.

Keep yourself at home and used mask when go outside and follows coughing etiquette. Furthermore, sample collection and transportation efforts will have to keep pace with the increased available testing capacity at the laboratories. This is the tough time to combat this outbreak and take necessary precaution and action to prevent future such type of pandemic state.

REFERENCES

1. Tyrrel DAJ, Almedia JD, Berry DM, Cunningham CH, Hamre D, Hofstad MS, Malluci L, McIntosh K. Coronavirus. Nature, 220, 1968, 650.
2. Ramadan N, Shaib H. Middle East respiratory syndrome coronavirus (MERS-CoV): A review. Germs, 9, 2019, 35-42. DOI: 10.18683/germs.2019.1155; PMID: 31119115
3. Zhong NS, Zheng BJ, Li YM, Poon , Xie ZH, Chan KH, et al. Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003, Lancet, 362, 2003, 1353-1358, DOI: 10.1016/s0140-6736(03)14630-2; PMID: 14585636.
4. World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. (2020, March 15) https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020.
5. Gorbalenya AE, Baker SC, Baric RS, Groot RJ de, Drosten C, Gulyaeva AA, et al. Severe acute respiratory syndrome-related coronavirus: The species and its viruses - A statement of the Coronavirus Study Group. bioRxiv, 2020, 1-15. https://doi.org/10.1101/2020.02.07.937862.
6. Rottier P, Sidell SG, Spaan WJM, Taguchi F, Talbot P. Coronaviridae, In Virus taxonomy. Classification and nomemclature of viruses. Accademic Press, San Diego, California, 2000, 835–849.
7. Woo PC, Lau SK, Lam CS, Lau CC, Tsang AK, et al. Discovery of seven novel mammalian and avian coronaviruses in Deltacoronavirus supports bat coronaviruses as the gene source of Alphacoronavirus and Betacoronavirus and avian coronaviruses as the gene source of Gammacoronavirus and Deltacoronavirus. J Virology, 6, 2012, 3995-4008. DOI: 10.1128/JVI.06540-11; PMID: 22278237
8. Luk HK, Li X, Fung J, Lau SK, Woo PC. Molecular epidemiology, evolution and phylogeny of SARS coronavirus. Infection, Genetics and Evolution, 71, 2019, 21-30. DOI: 10.1016/j.meegid.2019.03.001; PMID: 3084451.
9. Coronavirinae in Viral Zone (2019, March 23). https://viralzone.expasy.org/785
10. Lambeir AM, Durinx C, Scharpe S, De Meester I. Dipeptidyl-peptidase IV from bench to bedside: An update on structural properties, functions, and clinical aspects of the enzyme DPP IV. Crit Rev Clin Lab Sci, 40, 2003, 209-294. DOI: 10.1080/713609354; PMID: 12892317.
11. Chu H, Zhou J, Wong BH, Li C, Cheng ZS, Lin X, Poon VK, Sun T, Lau C C, Chan JF et al. Productive replication of Middle East respiratory syndrome coronavirus in monocyte derived dendritic cells modulates innate immune response. Virology, 2014, 454–455. DOI: 10.1016/j.virol.2014.02.018; PMID: 24725946.
12. Zhou J, Chu H, Li C, Wong BH, Cheng ZS, Poon VK, Sun T, Lau CC, Wong KK, Chan JY et al. Active replication of Middle East respiratory syndrome coronavirus and aberrant induction of inflammatory cytokines and chemokines in human macrophages: Implications for pathogenesis. J Infect Dis, 209, 2014, 1331-1342. DOI: 10.1093/infdis/jit504; PMID: 24065148.

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

13. **Dogra A, Bhawna G, Apoorav MS.** Corona Virus: A Novel Outbreak, Biomedical & Pharmacology Journal, 13(1), 2020, 5-10.

DOI: https://dx.doi.org/10.13005/bpj/1853.

14. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. Respirology, 23(2), 2018, 130-137. DOI: 10.1111/resp.13196; PMID: 29052924.

15. Gralinski L, Menachery V, Return of the Coronavirus: 2019-nCoV, Viruses 2020, 12(2), 135. DOI: 10.3390/v12020135; PMID: 31991541.

16. Hui DS, Azhar EI, Madani TA , Ntoumi F, Kock R, Dar O, Ippolito G. Mchugh TD, Memish Z, Drosten C, Zumla A, Petersen E. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health -The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis, 91, 2020, 264-266. DOI: 10.1016/j.ijid.2020.01.009; PMID: 31953166.

17. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, Spitters C, Ericson K, Wilkerson S, Tural A, Diaz G, Cohn A et al. First Case of 2019 Novel Coronavirus in the United States. N Engl J Med, 2020, 929-936. DOI: 10.1056/NEJMoa2001191

18. WHO. Emergencies preparedness, response. Pneumonia of unknown origin – China. Disease outbreak news (2020, February 5). https://HYPERLINK "http://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/" www.who.int/ csr/don/12-january-2020-novel-coronavirus-china/en/.

19. Xinhua. China's CDC detects a large number of new coronaviruses in the South China seafood market in Wuhan 2020, February 20). https://www.xinhuanet.com/2020-01/27/c_1125504355.html.

20. Li Q, Guan X,Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med, 382(13), 2020. DOI: 10.1056/NEJMoa2001316.

21. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report - 39. Geneva: WHO; 2020.

22. Coronavirus Outbreak (2020, February 23). https://www.worldometers.info/coronavirus/.

23. World Health Organization (2020, May 14). https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200514-covid-19-sitrep-115.pdf?sfvrsn=3fce8d3c_4

24. Covid-19 Statewise data, (2020, May 14). https://www.mygov.in/corona-data/covid19-statewise-status

25. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, 395, 2020, 497-506. DOI: https://doi.org/10.1016/S0140-6736(20)30183-5.

26. Wang Y, Wang Y, Chen Y, Qin Q: Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures, J Med Virol. 568-573, 2020. DOI: 10.1002/jmv.25748; PMID: 32134116.

27. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet, 395, 2020, 507-513. DOI: 10.1016/S0140-6736(20)30211-7; PMID: 32007143.

28. Coronavirus Outbreak (2020, February 23). https://www.worldometers.info/coronavirus/.

29. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected. Geneva: WHO; 2020. (2020, February 20). https://www.who.int/docs/default-source/coronaviruse /clinical-management-of-novel-cov.pdf.

30. Huaxia. WHO says vaccines against novel coronavirus 18 months away, pushes global research 2020 Xinhuanet. (2020, February 20). http://www.xinhuanet.com/english/2020-02/12/c_138777886.html.

31. Warren TK *et al.* Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. Nature, 531, 2016, 381-385. DOI: 10.1038/nature17180; PMID: 26934220.

32. Brown AJ et al. Broad spectrum antiviral remdesivir inhibits human endemic and zoonotic deltacoronaviruses with a highly divergent RNA dependent RNA polymerase. Antivir Res, 169, 2019. DOI: 10.1016/j.antiviral.2019.104541; PMID: 31233808.

33. Chu CM et al, Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax, 59(3), 2004, 252-256. DOI: 10.1136/thorax.2003.012658; PMID: 14985565

34. Jin YH et al: A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res, 7(1), 2020, 1-23. https://doi.org/10.1186/s40779-020-0233-6.

35. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet, 395, 2020, 473-475. DOI: 10.1016/S0140-6736(20)30317-2; PMID: 32043983.

36. Kui L, Fang YY, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl), 1-7, 2020. DOI: 10.1097/CM9.0000000000000744; PMID: 32044814.

37. Richardson P, Griffin I, Tucker C, et al. Baricitinib as potential treatment for 2019-nCoV acute respiratory disease. Lancet. 15-21, 2020. DOI: 10.1016/S0140-6736(20)30304-4; PMID: 32032529.

38. National Institutes of Health: novel coronavirus structure reveals targets for vaccines and treatments. (2020, March 11). https://www.nih.gov/news-events/nihresearch-matters/novel-coronavirus-structure-reveals-targets-vaccines-treatments.

39. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res, 30, 2020, 269-71. DOI: 10.1038/s41422-020-0282-0; PMID: 32020029.

40. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.

United States. N Engl J Med, 382, 2020, 929-936. DOI: 10.1056/NEJMoa2001191.

41. Chen Z.;Zhang W.; Lu Y *et. al.* From SARS-CoV to Wuhan 2019-nCoV Outbreak: Similarity of Early Epidemic and Prediction of Future Trends.: Cell Press 2020. DOI: https://doi.org/10.1101/2020.01.24.919241.

42. 2019 Novel Coronavirus. Prevention and Treatment (2020, February 20). https://www.cdc.gov /coronavirus /2019-ncov/about/ prevention-treatment.html.

43. Chang D, Xu H, Rebaza A, Sharma L, Cruz CSD. Protecting health-care workers from subclinical coronavirus infection. Lancet Respir Med, 2020, 8(3), PE13. DOI: 10.1016/S2213-2600(20)30066-7; PMID: 32061333.

44. World Health Organization. Advice on the use of masks the community, during home care and in health care settings in the context of the novel coronavirus (2019-nCoV) outbreak. Geneva: WHO; 2020.

45. World Health Organization. HAND HYGIENE: WHY, HOW & WHEN? Geneva: WHO; Revised August 2009, 1-7.

46. World Health Organization. International Health Regulations F. (2020, February 16). https://www.who.int/cholera/health_regulations/en/.

47. Ministry of Health and Family Welfare, Government of India. Revised travel advisory (2020, February 16). https://mohfw.gov.in.

48. Normile D. Coronavirus infections keep mounting after cruise ship fiasco in Japan (2020, February 28). https://www.sciencemag.org/news/2020/02/coronavirus-infections-keep-mountingafter-cruise-ship-fiasco-japan.

49. Horton R. Offline: 2019-nCoV-"A desperate plea". Lancet, 395, 2020, 400. DOI: 10.1016/S0140-6736(20)30299-3; PMID: 32035537.

50. Sands P, Mundaca-Shah C, Dzau VJ. The neglected dimension of global security - A framework for countering infectious-disease crises. N Engl J Med, 374, 2016, 1281-1287. DOI: 10.1056/NEJMsr1600236; PMID: 26761419.

51. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med, 382, 2020, 1177-1179. DOI: 10.1056/NEJMc2001737; PMID: 32074444.

52. GoK Dashboard. Kerala: COVID 19 battle (2020, March 31). https://dashboard.kerala.gov.in/index.php.

53. The Lancet Infectious Diseases. COVID-19, a pandemic or not? Lancet Infect Dis, 20(4), 2020, 383. DOI: 10.1016/S1473-3099(20)30180-8; PMID: 32178762.

54. World Health Organization. Coronavirus disease (COVID-19) advice for the public. WHO; 2020, (2020, March 22). https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-publi.

55. World Health Organization. Rational use of personal protective equipment for coronavirus disease 2019 (COVID-19): Interim guidance, 27 February 2020. WHO; 2020. (2020, March 22). https://apps.who.int/iris/bitstream/handle/10665/331215/WHO-2019-nCov-IPCPPE_use-2020.1-eng.pdf.

56. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): How to protect yourself. (2020, March 22). https://www.cdc.gov/coronavirus/2019-ncov/prepare/prevention.html.

57. World Health Organization. Home care for patients with COVID-19 presenting with mild symptoms and management of their contacts: Interim guidance, 17 March 2020. WHO; 2020. (2020, March 22). https://www.who.int/publicationsdetail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and management-of-contacts.

58. Zhonghua Liu, Xing Bing, Xue Za Zhi, Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China, 41, 2020, 145-151. DOI: 10.3760/cma.j.issn.0254-6450.2020.02.003; PMID: 32064853.

59. Su L, Ma X, Yu H, Zhang Z, Bian P, Han Y, et al. The different clinical characteristics of corona virus disease cases between children and their families in China - the character of children with COVID-19. Emerg Microbes Infect, 9, 2020, 707-713. DOI: 10.1080/22221751.2020.1744483; PMID: 32208917.

60. Indian Council of Medical Research. Note on COVID-19 laboratory preparedness in India. New Delhi: ICMR; 2020. (2020, March 17) 2020.

https://icmr.nic.in/sites/default/files/press_realease_files/ICMR_PressRelease_COVID_19,

61. Yadav PD, Potdar VA, Choudhary ML, Nyayanit DA, Agrawal M, Jadhav SM, et al. Full-genome sequences of the first two SARS-CoV-2 viruses from India. Indian J Med Res, 151, 2020. DOI: 10.4103/ijmr.IJMR_663_20; PMID: 32242873.

62. Indian Council of Medical Research. (2020, April 23)."SARS-CoV-2 (COVID-19) Testing: Status Update 23 April 2020, 09:00 AM IST" (PDF)

Source of Support: Nil, **Conflict of Interest:** None.

©Copyright protected. Unauthorised republication, reproduction, distribution, dissemination and copying of this document in whole or in part is strictly prohibited.