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REVIEW ON COVID-19

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ABSTRACT

The corona virus disease 2019 (COVID-19) is ongoing pandemic caused by SARS-CoV2. It was first identified in Wuhan, China in Dec 31, 2020. As of June 8, 2020, 69, 31,000 confirmed cases, 4, 00,857 confirmed death around 216 countries areas or territories with cases have been reported by WHO. The clinical trial of COVID-19 is going on Hydroxychloroquine, Azithromycin are given alone and combination and a new antiviral agent Ramdesivir help to some infection. However there is still no available vaccine and potential treatment for this corona virus. These COVID-19 pathogenesis pathways are still unknown. In this literature review we discussed about CoV, SARS-MERS CoV, COVID-19, Clinical manifestation, illness and risk factor, treatment, preventive measures, control the transmission.

KEYWORDS

Corona virus, SARS-MERS CoV, COVID-19, AYUSH Guideline, and Ayurvedic and Siddha formulation.

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INTRODUCTION

The Corona viruses are severe pathogen of human and animal. This novel corona virus was first identified as cluster of pneumonia cases in Wuhan city, Hubei Province, China in Dec, 2019¹. It easily spread throughout the China, followed spread to the other countries throughout the world due to highly contagious nature. The severe acute respiratory syndrome (SARS) corona virus, Middle East respiratory syndrome (MERS) corona virus and COVID-19 are separately discussed. Corona viridae

family viruses are single strand-RNA structure having 26 to 32 kilo bases length^{1,2}. These corona viruses produce mild or asymptomatic infection². However the severe acute respiratory syndrome (SARS CoV) corona virus and the Middle East respiratory syndrome (MERS CoV) corona virus produces lethal to human being^{3,4}. The most common symptoms were fever (83-99%), dry cough (59-82%) and tiredness. The less common symptoms are sore throat, diarrhoea, headache, body pain, conjunctivitis and loss of smell or taste. In this COVID-19 crises specific antiviral or vaccine are not available. But based on the Clinical trial report Hydroxychloroquine combination with Azithromycin, Ramdesivir, Ritonavir, Favipiravir and convalescent plasma therapy are given. Some Government hospital gives some Ayurvedic and Siddha formulation such as Nilavembu kudineer, Kabasura kudineer, Sitopaladi Churna, Tribhuvan Kirti and Sanjeevani Vati also given to improve the COVID-19 patient immunity⁵.

CoV

The First Human CoVs (HCoVs) was founded in 1965. The type of virus called as CoVs. Because the projection like surface which similar to crown⁶. This CoVs are 26 to 32kb lengthen positive strand RNA viruses. It causes the Severe Respiratory and neurological disease⁷. This CoV contains 4 genera such as Alpha, Beta, Gama and Delta. Out of 4 genera Alpha and Beta produces Human Respiratory illness⁷.

SARS and MERS

The SARS and MERS belong to the Beta CoVs which produce Severe Respiratory Syndrome⁸. SARS-CoV was first outbreak in Southern China in April 2003. It infected more than 3,000 people and killed 774 cases by 2004⁹. MERS-CoV was first identified in Jordan and it spread throughout the United Arab Emirates, was infected 2,465 people and killed 850 people by 2019⁹. Both these virus have an incubation period of 5 days. Then diseases develop within 13 days after virus enter⁷. The mortality rate for SARS-CoV is 10% while MERS-CoV is 36%^{10,11}.

COVID-19

The COVID-19 is new type of Beta-genera virus. This genetic sequence was similarity (96.2%) with Bat CoV strain (Bat -SL-CoV ZC45 and Bat-SL-CoVZXC21). This COVID-19 has 79.5% homology with SARS-CoV and 50% homology with MERS-CoV. It was originated from Bat species. But it crosses the animal, human species. In addition human to human transmission has been confirmed⁷. The mortality rate for COVID-19 was 2.9%¹². While 5.2 days incubation periods for COVID-19 extend to 14 days¹³.

COVID-19 STRUCTURAL AND PROTEIN NATURE

It is spherical shape under electron microscope, it have crown like projections on the surfaces of virus is called Spike (S) protein. This COVID-19 virus is covered by membrane (M) protein and also contains envelope (E) protein inside the viral envelope. The viral genomes are covered by Nucleocapsid protein¹⁴. The HCoV replicase gene consists of two overlapping open reading frames (ORFs)-ORF_{1a} and ORF_{1b}. ORF_{1a} is responsible for producing the poly protein pp_{1a}. ORF_{1b} is responsible for producing the poly protein pp_{1b}. The pp_{1a} and pp_{1b} involved autoproteolytic cleavage, and then gives 16 non-structural proteins (nsp1-16). Nsp₁ is the N-terminal cleavage polyproteins, which responsible for suppress of host IFN activity and protein synthesis. Nsp₃ encodes as two papain-like proteases (PLpro). Which are PLP₁ and PLP₂. PLP₁s are responsible for cleavage site 1 to release nsp1. While PLP₂ is responsible for cleavage sites 2 and 3 to release Nsp2 and Nsp3. Nsp5 is called as the corona virus main protease (Mpro) which essential for virus replication. The Nsp3, Nsp4, and Nsp6 are essential for remodeling of the cellular membranes Nsp7 and Nsp8 are act as cofactor for the RNA-dependent RNA polymerase (Nsp12) activity. The present study shows Nsp8 has RNA 3'-terminal adenylyl transferase (TATase) activity. Nsp9 are responsible for virus replication. It is a single-stranded DNA/RNA-binding protein, whereas Nsp10 is a Ds RNA-binding zinc-finger protein. Nsp7, nsp8, nsp9 and nsp10 are closely covered around the nsp12 (RNA-dependent RNA

polymerase). Nsp13 involved in the capping of viral RNAs. Nsp14 involved exoribonuclease (ExoN) activities and Nsp15 have an endoribonuclease (NendoU) activity, also IFN1 antagonist. Nsp16 protects viral RNA by 2'-O-methyltransferase activity¹⁴.

COVID-19 LIFE CYCLE

SARS-CoV-2 is get into bind human cells angiotensin- converting enzyme 2 (ACE2). After binding of ACE2, the COVID-19 virus is entered into cell through endocytosis (Figure No.2). This process is mediated by membrane bound protease. It is known as transmembrane serine protease 2 (TMPRSS2), which involved in cleaves the S protein for membrane fusion. Then the COVID-19 viral RNA genome is entering into the intracellular compartment. The viral RNA translated into the encoded structural and nonstructural proteins. The translation of the nonstructural proteins (Nsp1-16), replicas leads to in massive polypeptide chain, In which the 16 Nsp are cleaved. That process is regulated by host cell proteases, COVID-19 main protease and papain-like protease. On the other hand the RNA-dependent RNA polymerase (RdRp) involved in the replicate the viral genome. End of this process many structural and nonstructural proteins (Nsp1-16) are generated. This are accumulated to endoplasmic reticulum membrane. These are packed in Golgi apparatus for viral budding. Finally by exocytosis process it target to other host cell¹⁶.

CLINICAL MANIFESTATION

This COVID-19 shows the similar symptoms like SARS and MERS. Which mainly affect the respiratory tract at the upper air way with sneezing, rhinorrhea. Some of COVID-19 cases also asymptomatic nature¹⁷. The most common symptoms are fever (83-99%), dry cough (59-82%) and tiredness. The less common symptoms are sore throat, diarrhoea, headache, body pain, conjunctivitis and loss of smell or taste. The severe symptoms are shortness of breath¹⁸⁻²⁷, chest pain and loss of movement and speech²⁸. Up to 30% cases need ICU (Intensive Care Unit). As per the study reports the children's are not affected

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that much. Because they have low numbers of ACE-2 receptor in their respiratory air way system. Older people and co-morbidity patients with diabetes, cardiovascular diseases and asthma are very high risk for SARS CoV2^{29, 14}.

ILLNESS SEVERITY AND RISK FACTORS

The cohort study of COVID-19 in China conducted more than 44,000 patients. In this study 81% patients were mild to moderate; 14% patients with severity; 5% patients with critical situation. Overall fatality rate was 2.3% while critical severity was 49% fatality rate¹⁹. According to this study 14.8% fatality rate for >80 years old; 8.0% fatality rate for 70-79 years old; 3.6% fatality rate for 60-69 years old; 1.3% fatality rate for 50-59 years old; 0.4% fatality rate for 40-49 years; 0.2% fatality rate for <40 years old^{19, 20}. Then 10.5% fatality rate for those with Cardiovascular diseases; 7.3% fatality rate for those with diabetes and 6% fatality rate for those with chronic respiratory diseases, hypertension and cancer²⁰.

TREATMENT

The COVID-19 was ongoing pandemic. Still no specific vaccination and Antiviral treatment are available like SARS and MERS CoV¹³. There is no FDA approved drug for the treatment of COVID-19¹⁸. According to the ICMR (Indian Council of Medical Research) Lopinavir/Ritonavir (200mg/50mg) tablet twice daily and if the patient unable to take medicine by mouth Lapinavir 400mg/ Ritonavir 100mg -5ml suspension twice daily). According to the Tamil Nadu Ministry of Health and Family Welfare says the COVID-19 treatment include Tab. Azithromycin 500mg once daily for 5 days. Tab. Hydroxychloroquine 400mg on day 1 followed by 200mg BD X 4 days. Cap. Omeprazole 40mg BD X 5 days. Tab. Ondansetron 4mg BD X 5 days. Zinc and Vitamin C supplements. Tab. Paracetamol 500mg TDS or SOS. Avoid NSAIDs, steroids, nebulisation, use metered dose inhalers if necessary^{23,26,27}. The plasma convalescent therapy also performed in several hospitals. It gives good results. The IL6

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inhibitors (Siltuximab) also underwent phase 2/3 clinical trial to treat COVID-19. Now Favipiravir is an antiviral drug as new face. It is initially identified as Antiflu in Japan. In line with this strategy, Glen mark proposes to combine two antiviral drugs Favipiravir (Approved drug for novel flu pandemics) with Umifenovir (Approved drug for Influenza) - safety well established. Now it is identified as treatment for Corona virus. It was already administered to 2050 patients in Japan with more recovery rates at 7 to 14 days treatment in mild to moderate patients. It already approved in Italy, China, Canada and India. It mainly acts on RNA Dependent RNA Polymerase of COVID-19. The inhibition of RNA Dependent RNA Polymerase leads to inhibition of the viral replication³¹.

PREVENTIVE MEASURES

The ministry of AYUSH department says to take Chyavanprash (10gm) in the morning, Then recommended to take herbal decoction (Kadha) prepared from Basil (Tulsi), Cinnamon (Dalchini), Black pepper (Kalimirch), Dry Ginger (Shunthi) and Raisin (Munakka) twice a day³². Then take sesame oil, coconut oil or ghee are drop by the noses (Pratimarsh Nasya) in early morning and evening. Also intake of 1 table spoon of sesame oil or coconut oil in mouth for 3 minutes with warm water rinse and spit it out. Steam inhalation with fresh Mint (Pudina) leaves, Caraway seeds (Ajwain) can be added to the daily food. The Clove (Lavang) powder mixed with natural sugar / honey can be in case of throat irritation or cough. In India the first plant- derived drug, AQCH (Sun Pharma's formulation) was approved for clinical trial by Drug Controller General of India (DCGI) to treat COVID-19. This ACQH derived from tropical plant *Cocculus hirsutus*. Which shows broad spectrum antiviral activity in *in vitro* study⁵.

Our government gives following preventive measures to beat COVID-19. These are Stay away, Hygiene, Social distancing, Additional care is to be observed in case of elderly and children, DIET,

Exercise and meditation, Adequate sleep and usage of adequate Personal Protective Equipment (PPE).

TREATMENT OF PNEUMONIA

According to Ministry of Ayush the following ayurvedic medicine are recommended to pneumonia. Sanjeevanivati - 125mg TDS/ Gorochanadivati - 125mg TDS with luke warm water; Somasav/Pushkaramoolasava-10 - 20ml with equal amount of water BD; Talisadi (4g) + Madhuyashtichurna (2gms) + Sameerapannaga rasa 125 mg- twice in a day with honey/ luke warm water; Pushkaramoolasava 15 - 20ml BD/TDS with equal water; Agastya Haritaki/Vyaghriharitaki/ Chitrakaharitaki Avaleha-10 - 12gm BD after food with water; Kantakariavaleha 10 - 12gm BD after food 7. Dashamoolakatutrayadi Kashaya 20 - 30ml TDS with water before food 8. Vasakasava 15-20ml TDS with water after food; Bharangyadikwatha 30-40ml BD before food; Chandramrita rasa - 250mg BD with honey or Tamboolaswarasa or Aasa swarasa or Ardrakaswarasa.

TREATMENT OF ACUTE RESPIRATORY DISTRESS SYNDROME

According to Ministry of Ayush the following ayurvedic medicine are recommended to Acute Respiratory Distress Syndrome. Inhalation with Karpoora and Nilgiritaila; ShwasKuthar Rasa (125 - 250mg) with Kantakari (2g) and pippalichurna (1gm) given with mustard oil and jiggery; Mallasindoora 125mg + Talisadichurna 3gms + Shringabhasma 125mg + Abhrakabhasma 125mg, with honey BD after food; Local application of Saindhavaditaila to chest followed by Nadiswedana.

TREATMENT OF IMMUNOCOMPROMISED CONDITIONS

According to Ministry of Ayush the following ayurvedic medicine are recommended to Immuno compromised conditions. Samshamani Vati 500mg tablet, 2 tablet BD after food; Agastya Haritaki Rasayana 10 - 12gm BD after food; Chitraka Haritaki Rasayana 10 - 12gm BD after food;

Chayavanaprashavaleha 10 - 12gm BD after food;
Bramha Rasayana 10 - 12gm BD after food.

CONTROL THE TRANSMISSIONS

According to the Tamil Nadu Government Health and family welfare recommended the following Drug and Herbal powder to person who is in COVID-19 duty - Tab Zinc 150mg once daily for ten days and Nilavembu kudineer and Kaba sura kudineer extraction with empty stomach for one month. It is 60ml for Adult and 30ml for children. Lysol sprays for disinfectant Lysol IP 50% and liquid soap 50%. Alternatively 1% Hypochlorite solution can be used. Hand sanitizer contains Iso Propyl Alcohol (75%), Glycerol (1.45%) and Hydrogen Peroxide (0.125%)²⁴. Social distancing is the best precautionary measures to control COVID-19.

Table No.1: Immunity Enhancers - Single Drugs (Ministry of AYUSH)¹⁶

S.No	Immunity Enhancers	Single Drugs
1	Guduchi	500 to 1000mg of aqueous extract of Guduchi (<i>Tinospora cordifolia</i> (Thunb. Miers)
2	Amla	Fresh Amla fruit (Indian gooseberry - <i>Emblicca officinalis</i> L/ <i>Phyllanthus emblica</i> L) or Amla candy is also advisable
3	Haridra Garglin	Haridra Gargling with warm water added with turmeric powder (<i>Curcuma longa</i> L) and a pinch of salt or Turmeric (<i>Curcuma longa</i> L)
4	Tulasi	Sipping of water processed with Tulsi (basil leaves - <i>Ocimum tenuiflorum</i> L Merr (synonym <i>Ocimum sanctum</i> L)
5	Ashwagandha root powder	Root powder 3-5gm twice a day with warm milk or water/ ashwagandha extract 500mg twice a day with warm water

Table No.2: Immunity Enhancers - Formulations (Ministry of AYUSH)¹⁶

S.No	Immunity Enhancers -Formulation	Dose
1	Chyawanprash avaleha	10 - 12gm/1 Spoon
2	Drakshavaleha	10 - 12gm/1 Spoon
3	Indukantam grutham	10 - 12gm twice daily before food, when hungry
4	Aravindasava	15 - 20ml with equal quantity of warm water after food
5	Balachaturbhadra churna	1 - 2gm with honey
6	Haridra khanda	3 - 5gm intermittently with honey/warm water

Table No.3: Management Guidelines for Severe Symptoms Disclaimer¹⁶

S.No	Ayurvedic Medicine	Treatment	Prescribed Dose
1	Maha Sudarshangan Vati	Fever	500mg TDS with lukewarm water
2	Amritarista	Fever	15-20ml tid with water after food
3	Amritottara Kashaya	Fever	15ml tid with water before food
4	Vishamajwarantakalauha	Fever	with gold - 125mg bid with water - High fever with debility
5	Mrityunjaya rasa	Fever	125mg tid with water - Uncontrolled fever with myalgia
6	Samshamanivati	Fever	500mg, 2 tab BD after food
7	ArkaYavani	Fever	10 - 25ml QID with water - Deepanapachana Jwara, Aruchi
8	Pathyadi Kashayam/Guduchyadi Kashayam/Bharangyadi Kashaya	Fever	freshly prepared 30 - 40ml BD before food
9	Chaturthaka Jvaraharakwatha	Fever	Giloya stem either dry or wet -5gms+ Amalaki-Dry-5gms + Nagarmotha-5gms decoction with 200ml of water and reduced it up to 100ml
10	Tribhuvanakirti rasa	Fever	125mg BD after food with shunthijala or water
11	Bilwativati	Fever	1 TDS
12	Vyoshativati/ Lavangadi Vati/ Khadirativati	Sore throat	2 tab TDS
13	Laxmivilasa rasa	Sore throat	125mg tid with tamboolaswarasa after food
14	Haridrakhand	Nasal congestion	3 - 5gm BD with lukewarm water/ milk
15	Laxmivilasa rasa	Nasal congestion	125 - 250mg BD with tamboolaswarasa after food
16	Rasnasaptak	Myalgia	Kwath- 30 - 40ml BD before food
17	Ashwagandharista	Myalgia	15 - 20ml BD with water
18	Balarishta	Myalgia	15 - 20ml BD with water
19	Devadaryadikwatha	Myalgia	30 - 40ml BD before food
20	Dashamoolakwath	Myalgia	30 - 40ml BD before food
21	Godantibhasma	Myalgia	500mg - 1gm BD/TDS daily with ghee, sugar, warm milk or water
22	Talisadi Churna	Cough	Talisadi Churna (4g) + Madhuyashtichurna (2g) BD with honey/ lukewarm water
23	Sitopaladichurna	Cough	3-6 gm with honey BD/ TDS or as required
24	Tankanabhasma	Cough	250 - 500mg BD
25	Dashamoolakatutrayadi Kashaya	Cough	20 - 30ml TDS with water before food
26	Shadangapaneeya	Dehydration	40ml tid/as per requirement

Table No.4: Anti-viral Siddha Formulation (Ministry of AYUSH)³³

S.No	Siddha medicine	Dose
1	Kaba Sura Kudineer (Formulation)	60ml twice a day after food
2	NilaVembu Kudineer (Formulation)	60ml twice a day after food
3	Visha Sura Kudineer (Formulation)	60ml twice a day after food
4	Pavala Parpam (Formulation)	-100mg twice a day with Honey
5	Velli parpam (Formulation)	50 to 100mg twice a day with Honey
6	Inji (Zingiber officinale)	Injisurasam- 10ml Once a day
7	Thulasi (Ocimum sanctum)	Thulasi Kudineer- 60ml Twice a day
8	Milaku (Piper nigrum)	With Thulasi as Kudineer said above
9	Karunjeerakam (Nigella sativa)	Karunjeeraka Chooranam 1gm BD
10	Keezhanelli (Phyllanthus niruri)	Keezhanellisamoolam- 2gm Twice a day
11	Athimadhuram (Glycyrrhiza glabra)	Athimadhura Chooranam- 1gm BD
12	Vellaipoondu (Allium sativum)	Poonduthaen
13	Citra mutti (Sidacordifolia)	Citramutti Kudineer-30ml Twice a day
14	Seenthil (Tinospora cordifolia)	Seenthil Chooranam– 1gm Twice a day
15	Manjal (Curcuma longa)	Take sufficient amount
16	Elumitchai (Citrus limonia) Volatile oil	Take sufficient amount
17	Vembu (Azadirachta indica)	Take sufficient amount

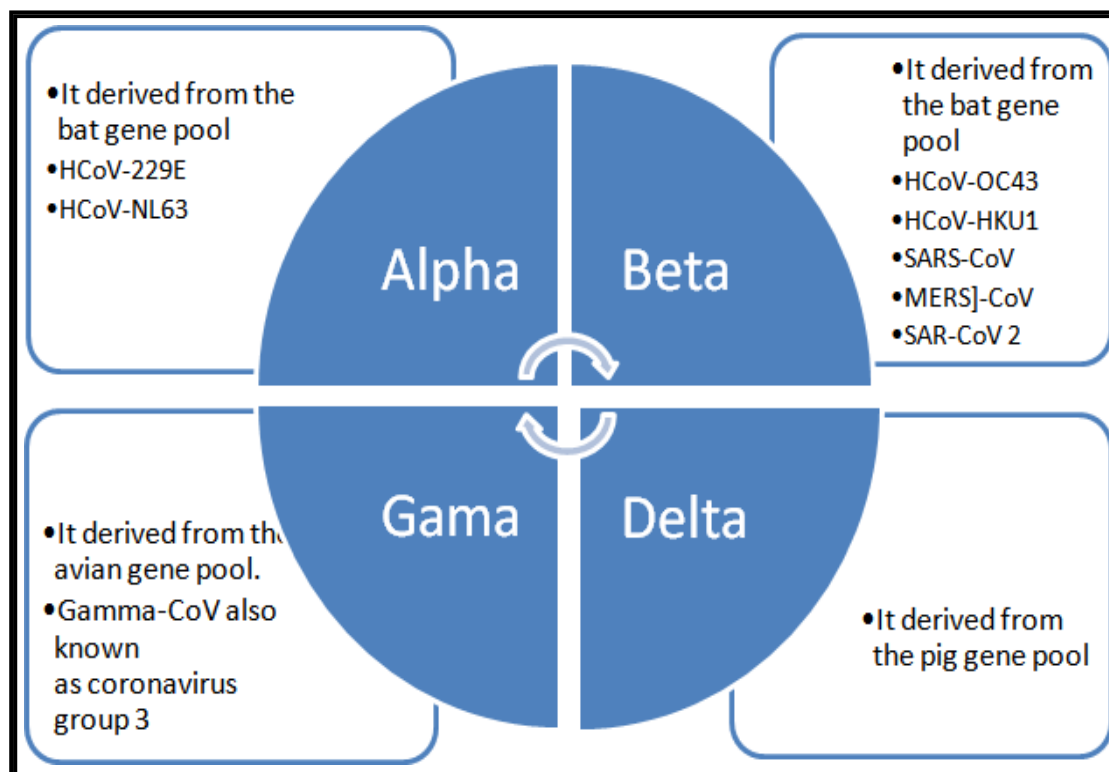


Figure No.1: Corona virus families are four genera-Human respiratory illness producing species (Alpha and Beta)

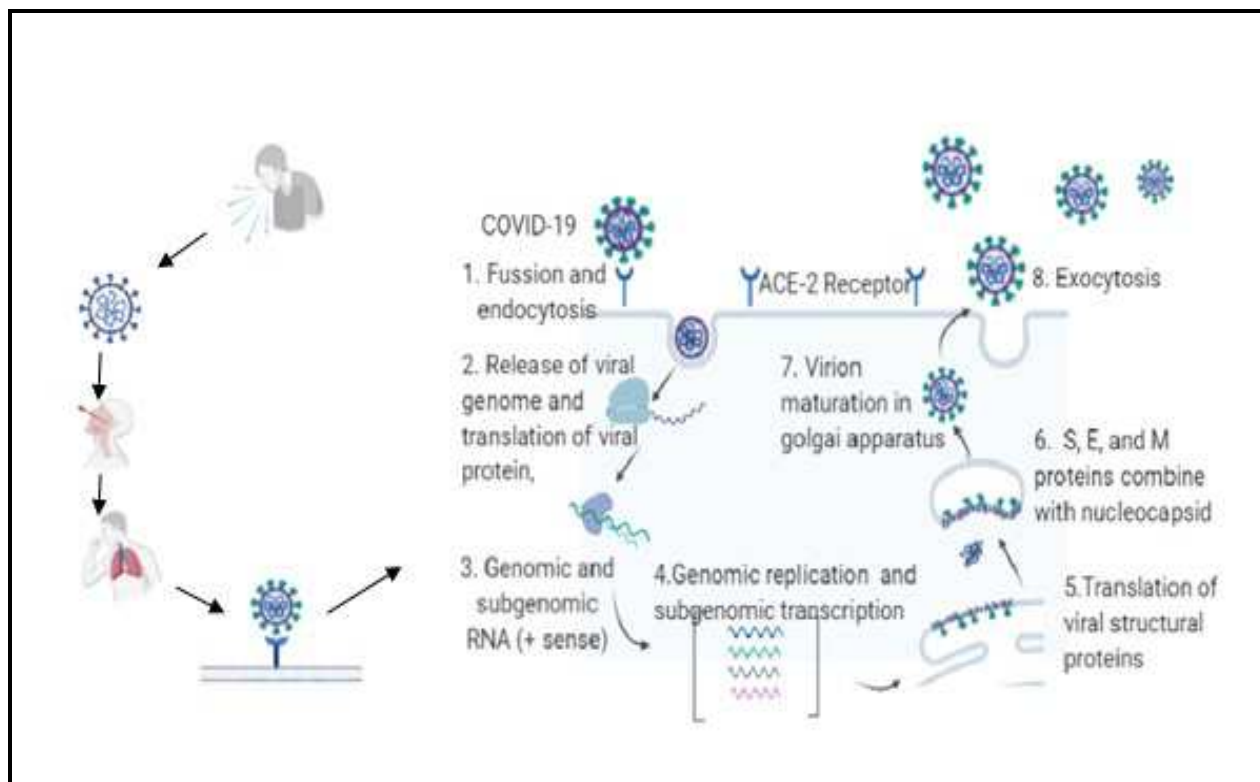


Figure No.2: COVID-19 Life cycle¹⁵

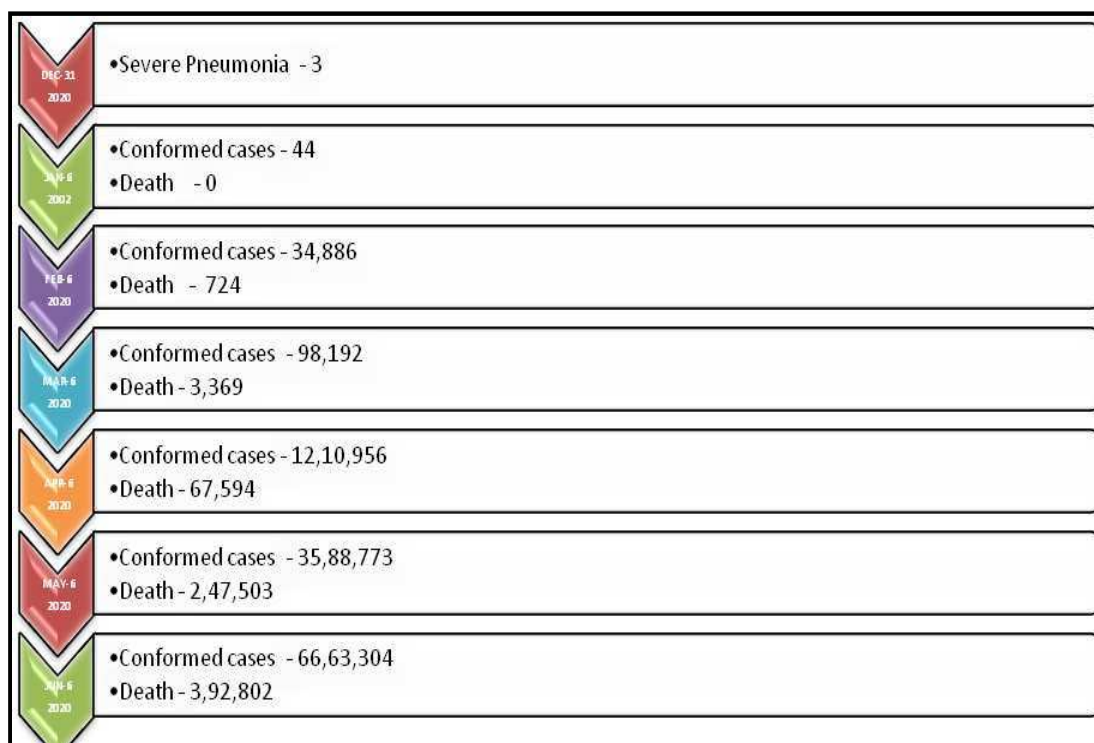


Figure No.3: According to WHO report - Globally COVID-19 affected Cases (Source- WHO)³⁰

CONCLUSION

This COVID-19 outbreak has very challenged to the economic, medical and public health infrastructure to the all countries. The time alone will tell how the COVID-19 will impact our lives here in our India. For the COVID-19 treatment should be mixture of allopathic treatment, sometime ayurvedic and non pharmacological treatment ultimate to manage the crises. But for the ayurvedic treatments haven't sufficient scientific based evidence. It is only having practice based evidence. However the self-discipline and social distancing are the best precautionary measures to control the spreading. I hope this literature review give some awareness and precautionary measures.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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