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Corona Virus (Covid-19) Pandemic: A Systematic Review

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Abstract

The recently emerged CORONAVIRUS (COVID-19) is now considered as a pandemic threat worldwide. It is novel class of virus that affects the respiratory tract and leads to difficulty in breathing. The virus originated in bats and was transmitted to humans. It has been known to infect human hosts and cause respiratory diseases. Currently, there is still dearth of information on foremost source of viral transmission along with exact pathogenic mechanism of action. Besides this, the hospital outbreak of super-spreading virus has made a greater concern about global health due to SARS-CoV and MERS-CoV which are highly pahogenic. There have been around 1,519,503 reported cases of coronavirus disease worldwide and 88,549 reported deaths along with 3,30,916 total recovered patients to date (9/4/2020).The disease is transmitted by inhalation of infected droplets .The symptoms are usually fever, sputum production, nasal congestion, pneumonia, sore throat ,breathlessness. Diagnosis of disease is done by routine lab findings, specimen examination using RT-PCR and by using diagnostic kits. Prevention entails regular hand washing, covering mouth and nose and home isolation of suspected cases. Treatment is usually supportive of ayurvedic, herbal medicines and allopathic combinations mostly antiviral drugs. This revelation may exert crucial guidance for understanding the viral infection and measures to prevent and treat infection.

Keywords: COVID -19, Respiratory infection, Pneumonia, SARS-CoV, MERS-CoV.

INTRODUCTION

Coronaviruses are a group of enveloped viruses with nonsegmented, single-stranded, and positive sense RNA genomes. Apart from infecting a variety of economically important vertebrates (such as pigs and chickens), six coronaviruses have been known to infect human hosts and cause respiratory diseases. Among them, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are zoonotic and highly pathogenic coronaviruses that have resulted in regional and global outbreaks. According to the International Committee on Taxonomy of Viruses, coronaviruses are classified under the order Nidovirales, family Coronaviridae, subfamily Coronavirinae. Based on early serological and later genomic evidence, Coronavirinae is divided into four genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus[1]

The updated classification scheme of HCoV and other coronaviruses[1]

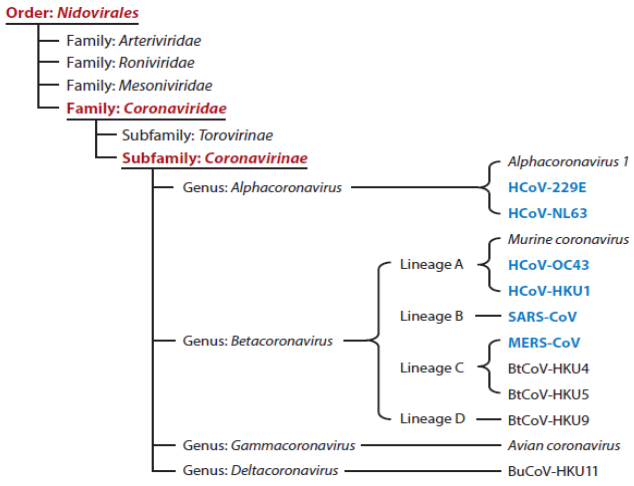


Fig. 1: Taxonomy of HCoVs: the updated classification scheme of HCoV and other coronaviruses

The six known HCoVs are in blue. Abbreviations: BtCoV, bat coronavirus; BuCoV, bulbul coronavirus; HCoV, human coronavirus; MERS-CoV,Middle East respiratory syndrome coronavirus; SARS-CoV, severe acute respiratory syndrome coronavirus.

PAST HISTORY

Human coronaviruses were first discovered in the late 1960s.The earliest ones discovered were an infectious bronchitis virus in chickens and two in human patients with the common cold (later named human coronavirus 229E and human coronavirus OC43).Other members of this family have since been identified, including SARS-CoV in 2003, HCoV NL63 in 2004, HKU1 in 2005,

A newly emerged highly pathogenic beta-coronavirus called Middle East Respiratory Syndrome Coronavirus (MERS-CoV) formerly known as HCoV-EMC (Human Coronavirus Erasmus Medical Center) was recognized as the causal agent of 50% lethality and fatal respiratory disease in humans during 2012.[2] As the first case was detected on June, 2012 in Saudi Arabia and the next was in Qatar where a 49 years old man was infected by the novel coronavirus (MERSCoV) in September 2012 and there was a 99.5% sequence match between the two viruses separated from the patients. The viral transmission from discriminating animal species to human has been evidenced and another study has also demonstrated that the pathogen has spread worldwide largely by human to human infection.[3]Globally, since September 2012, WHO has been alerted about 1,595 laboratory-confirmed cases of infection with MERS-CoV, including at least 571 related decease. Till August 2015, 498 deaths were found among 1165 cases in the Saudi Arabian territory (ECDC 2015).[4,5] SARS-CoV2 (formerly known as 2019-nCoV) was found in 2019. Most of these have involved serious respiratory tract infections.[6]

SOURCES OF INFECTION AND TRANSMISSION ROUTES

Respiratory infections can be transmitted through droplets of different sizes: when the droplet particles are >5-10 µm in diameter they are referred to as respiratory droplets, and

when then are <5µm in diameter, they are referred to as droplet nuclei.[7] According to current evidence, COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes.[8-13] In an analysis of 75,465 COVID-19 cases in China, airborne transmission was not reported.[14]

Droplet transmission occurs when a person is in in close contact (within 1 m) with someone who has respiratory symptoms (e.g., coughing or sneezing) and is therefore at risk of having his/her mucosae (mouth and nose) or conjunctiva (eyes) exposed to potentially infective respiratory droplets. Transmission may also occur through fomites in the immediate environment around the infected person.[14] Therefore, transmission of the COVID-19 virus can occur by direct contact with infected people and indirect contact with surfaces in the immediate environment or with objects and surfaces used on the infected person (e.g., stethoscope or thermometer).[15]

Scientists still don't think surfaces are the main way the virus spreads, but it is possible to catch the virus by touching a surface with the virus there, then touching your face. The coronavirus can live on soft surfaces for 24 hours, and hard ones for 48 hours. keys can host the coronavirus for 48 hours . Touching door handles, and other similar hard surfaces, has a risk of transmission for up to 72 hours. The coronavirus could spread in gyms, where people are in close quarters and share equipment.[16]

There is some evidence that COVID-19 infection may lead to intestinal infection and be present in faeces. However, to date only one study has cultured the COVID-19 virus from a single stool specimen.[15] There have been no reports of faecal−oral transmission of the COVID-19 virus to date.[15]

GENOME ORGANIZATION

Morphology and Genomic Structure of HCoV

Coronaviruses are spherical or pleomorphic, with a diameter of 80–120 nm. Under the electron microscope, the virion surface is decorated with club-like projections constituted by the trimeric spike (S) glycoprotein [17]. Shorter projections made up of the dimeric hemagglutinin-esterase (HE) protein are observed in some betacoronaviruses (such as HCoV-OC43 and HCoV-HKU1).[18] Both S and HE are type I transmembrane proteins with a large ectodomain and a short endodomain. The viral envelope is supported by the membrane (M) glycoprotein, themostat abundant structural protein that embeds in the envelope via three transmembrane domains.[17] Additionally,a small transmembrane protein known as the envelope (E) protein is also present in a low amount in the envelope.[19] Finally, the nucleocapsid (N) protein binds to the RNA genome in a beads-on-a-string fashion, forming the helically symmetric nucleocapsid.[17]

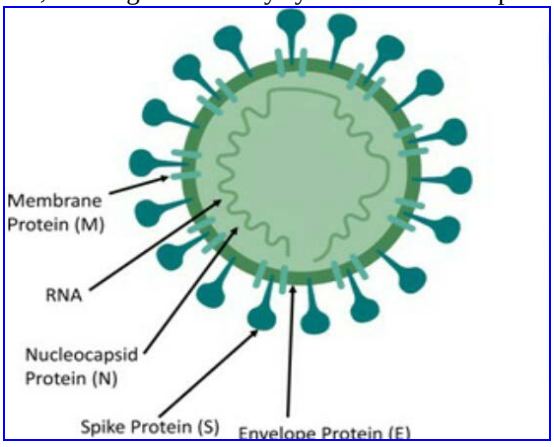


Fig. 2: Overview of coronavirus

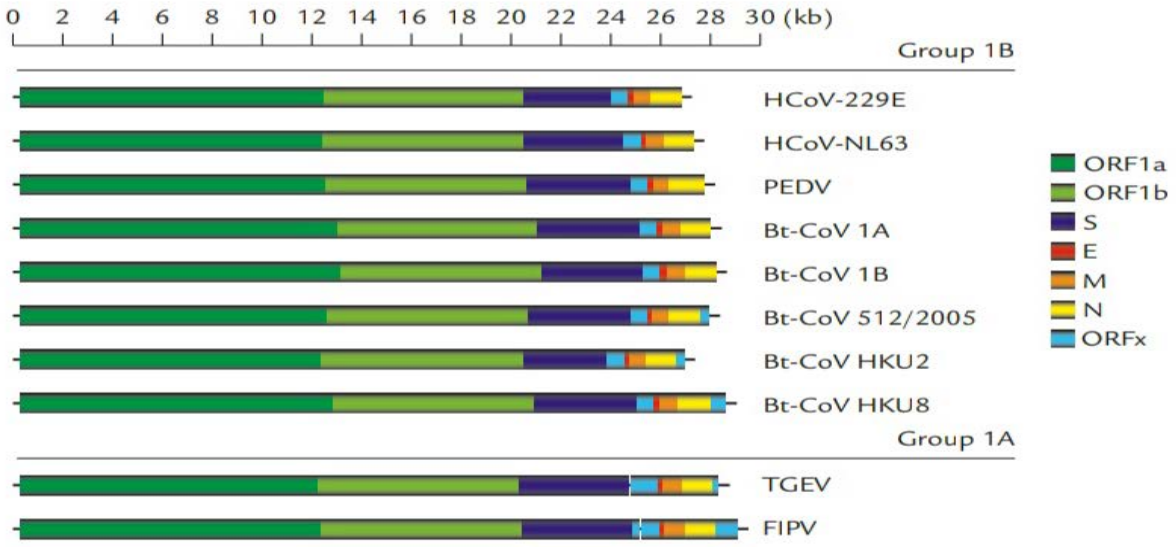


Fig. 3: Schematic representation of the genomic organization of group 1 coronaviruses (CoVs)

Group 1B CoVs HCoV-229E (NC002645), HCoV-NL63 (NC005831), porcine epidemic diarrhea virus (PEDV; NC003436), bat coronavirus 1A (Bt-CoV 1A; NC010437), Bt-CoV 1B (NC010436), Bt-CoV 512/2005 (NC009657), Bt-CoV HKU2 (NC009988) and Bt-CoV HKU8 (NC010438), and group 1A CoVs porcine transmissible gastroenteritis virus (TGEV; NC002306) and feline infectious peritonitis virus (FIPV; NC007025) genome organization. The open reading frames (ORFs) are denoted as replicase 1A (ORF1a), replicase 1B (ORF1b), S, E, M, N and accessory genes (ORFx). Human coronavirus 229E and NL63 close yet still so far.

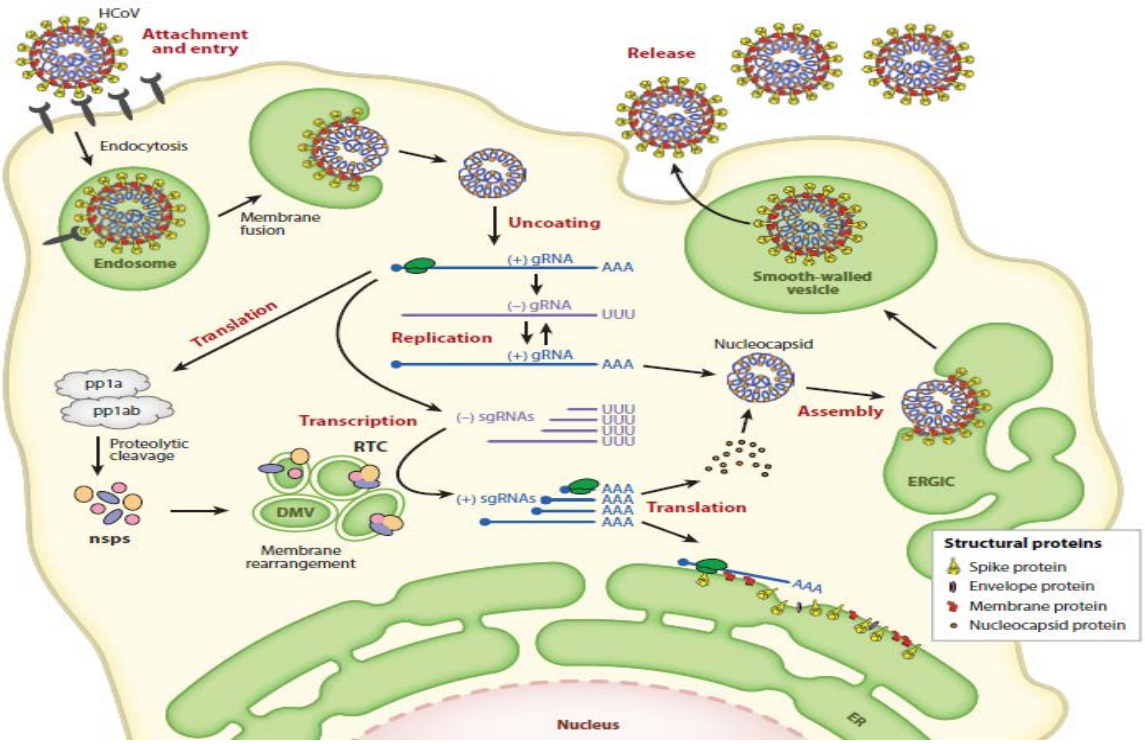


Fig. 4: Replication cycle of human coronaviruses (HCoVs)

Schematic diagram showing the general replication cycle of HCoVs. Infection starts with the attachment of HCoVs to the cognate cellular receptor, which induces endocytosis.Membrane fusion typically occurs in the endosomes, releasing the viral nucleocapsid to the cytoplasm. The genomic RNA (gRNA) serves as the template for translation of polyproteins pp1a and pp1ab, which are cleaved to form nonstructural proteins (nsps). nsps induce the rearrangement of cellular membrane to form double-membrane vesicles (DMVs), where the viral replication transcription complexes (RTCs) are anchored. Full-length gRNA is replicated via a negative-sense intermediate, and a nested set of subgenomic RNA (sgRNA) species are synthesized by discontinuous transcription. These sgRNAs encode viral structural and accessory proteins. Particle assembly occurs in the ER-Golgi intermediate complex (ERGIC), and mature virions are released in smooth-walled vesicles via the secretory pathway.

STAGES

1) The first stage (Sporadic cases)

This stage involves important cases and little transmission .During the early stage of the outbreak, the main strategy focused on preventing the exportation of cases from Wuhan and other priority areas of Hubei Province, and preventing the importation of cases by other provinces; the overall aim was to control the source of infection, block transmission and prevent further spread. The response mechanism was initiated with multi-sectoral involvement in joint prevention and control measures. Wet markets were closed, and efforts were made to identify the zoonotic source. Information on the epidemic was notified to WHO on 3 January, and whole genome sequences of the COVID-19 virus were shared with WHO on 10 January. Protocols for COVID-19 diagnosis and treatment, surveillance, epidemiological investigation, management of close contacts, and laboratory testing were formulated, and relevant surveillance activities and epidemiological investigations conducted. Diagnostic testing kits were developed, and wildlife and live poultry markets were placed under strict supervision and control measures.

Important Measures

a) Good hand hygiene and cleaning.
b) Early detection and isolation.
c) Contact tracing.
d) Limit travel from some areas.

2) The second stage (Clusters)

This stage involves important cases and new cases in local clusters. During the second stage of the outbreak, the main strategy was to reduce the intensity of the epidemic and to slow down the increase in cases. Measures were taken to ensure that all cases were treated, and close contacts were isolated and put under medical observation. Public risk communications and health education were strengthened; allocation of medical supplies was coordinated, new hospitals were built, reserve beds were used and relevant premises were repurposed to ensure that all cases could be treated; efforts were made to maintain a stable supply of commodities and their prices to ensure the smooth operation of society.

Important Measures

a) Good hand hygiene and cleaning.
b) Early detection and isolation.

3) The third stage (Main Wave)

This stage involves widespread transmission in society. The third stage of the outbreak focused on reducing clusters of cases, thoroughly controlling the epidemic, and striking a balance between epidemic prevention and control, sustainable economic and social development, the unified command, standardized guidance, and scientific evidence-based policy implementation .

Important measures

a) Social distancing.

4) The fourth stage (Full Epidemic)

This stage involves pressure on healthcare service

Important Measures

a) Social distancing.

5) The fifth stage (Late Epidemic)

This stage involves declining in number of cases.

Important Measures

a) Good hand hygiene and cleaning.

b) Social distancing.[20]

CASE FINDING

Human Coronaviruses (h CoV) belonged to alpha and beta genera. Since the first report of h CoV isolation in 1966, h CoV group has been repeatedly confirmed as an important and frequent cause of common cold, exacerbation of asthma, contributors to lower respiratory tract infections in children and elderly and diarrhea in some. Human CoV are found worldwide and predominantly are active in winter and early months of spring in temperate climates [21,22]. In November 2002, a novel coronavirus was found to be responsible for a global outbreak of an Acute Severe Respiratory Syndrome (SARS) as the prominent symptoms. The outbreak spread worldwide from its origin in China and probably represented transmission from an animal species, possibly bats to human. The novel virus named as SARS related Coronavirus (SARS r-CoV), ended after 9 months.[21] More recently, in 2012, a highly pathogenic novel CoV appeared in Saudi Arabia and neighbor countries named as Middle East Respiratory Syndrome Coronavirus (MERS)[2,23] This virus with a case fatality of approximate 50% and ability to spread at least to a limited extent in families and among patients and health care workers in hospitals, originated from an animal source, possibly camels.[24-28]

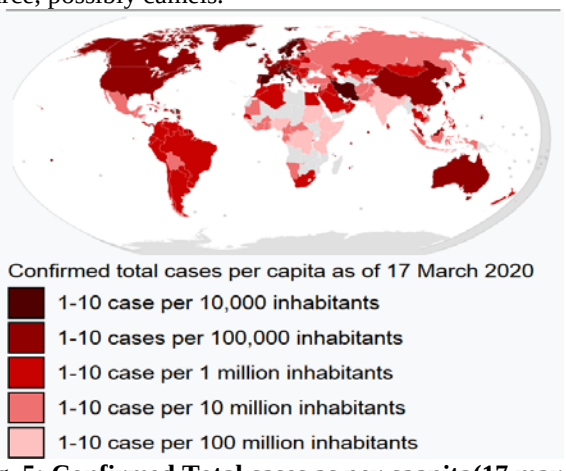
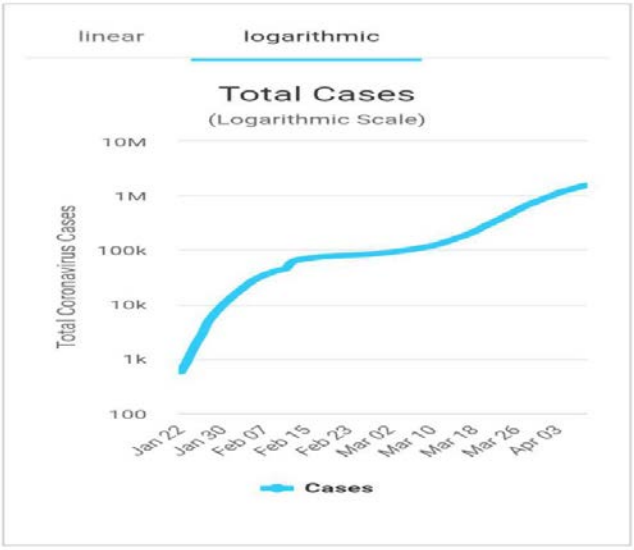


Fig. 5: Confirmed Total cases as per caapita(17 march 2020)



Graph 1: Totol Cases (Jan22-Apr 03)

Graph 2: Total Deaths (22 jan-April 03)

Table No. 1: Confirmed Total Cases Per Capita as of 9 APRIL 2020[29]

Countries or Territory	Total Cases	Total Deaths	Total Recoveries
USA	4,35,393	14,806	22,891
Spain	1,48,220	14,792	48,021
Italy	139,422	17,669	26,491
France	112,950	10,869	21,254
China	81,928	3,337	77,370
Iran	64,586	3,993	29,812
India	5,916	178	506

SYMPTIOMS [30]

1) fever (38.5 degrees or above)
2) Sneezing
3) Dry Cough
4) Fatigue
5) Sputum Production

6) Muscle Pain
7) Sore throat
8) Chills
9) Nasal congestion
10) Diarrheoa
11) Haemoptysis
12) Conjuctivital congestion.
13) Elevated Creatine kinase
14) Pneumonia
15) Decreased Lymphocytes

TESTING AND DIAGNOSIS

1. Routine labs

In early phase of the disease, WBC counts are normal or low, lymphocyte counts are low, and some patients may have elevated AST/ALT, LDH, CK and myoglobin levels. Critically ill patients may have elevated troponin. The majority of patients have an elevated CRP and ESR, a normal procalcitonin level. Severe cases have an elevated d-dimer, a progressively decreasing lymphocyte count. Severe and critical cases often have elevated levels of inflammatory markers.

2. Specimen and serology

Specimen: When examined using RT-PCR or NGS (next generation sequencing),viral nucleotides can be detected from swab samples obtained from nasopharynx, sputum, lower respiratory tract secretions, blood serum, and stool. Samples obtained from lower respiratory tract (sputum or bronchial lavage) yield more consistent results. These samples should be sent to the lab for testing expeditiously.

Serology: IgM becomes positive 3-5 days after symptom onset, IgG titers in the recovery phase have a minimum of 4-time increase from acute phase.

3. Chest imaging

In early phase, small patchy infiltration and interstitial changes can be seen, especially in the periphery of the lung. Then rapidly progressing to bilateral multifocal ground glass opacities and infiltrations. Severe cases can have consolidation of lung parenchyma. Pleural effusion is rarely seen.

4. Procedure

Sample collection, RT-PCR, and interpretation of results was done as previously described. Two sets of primers were used for two target genes (ie, open reading frame 1ab [ORF1ab] and nucleocapsid protein [N]) according to the protocol issued by the National Institute for Viral Disease Control and Prevention in China (panel 1).

Panel 1

Primers for targets

Target 1: open reading frame 1ab (ORF1ab)
Forward primer: CCCTGTGGGTTTTACACTTAA
Reverse primer: ACGATTGTGCATCAGCTGA
Probe: 5′-VIC-CCGTCTGCGGTATGTGGAAAGGTTATGG-BHQ1-3′
Target 2: nucleocapsid protein (N)
Forward primer: GGGGAACTTCTCCTGCTAGAAT
Reverse primer: CAGACATTTTGCTCTCAAGCTG
Probe: 5′-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3′

On admission, patients were assessed for clinical type, according to guidelines for scoring paediatric patients with COVID-19 (recommendations issued by the paediatrics branch of the Chinese Medical Association; panel 2). The therapeutic principles included general support therapy; monitoring of lung, liver, kidney, and myocardial functions; active control over high fever; oxygen uptake if necessary; and antiviral treatment with interferon alfa and lopinavir–ritonavir. Treatment outcomes were defined as improved, cured, and failed. Improved outcome referred to the end of fever and improvement in pneumonia (via CT scan) and improvement in upper respiratory manifestations. Cured outcome referred to normal body temperature for 3 days, plus improved outcomes and two negative results on RT-PCR for SARS-CoV-2. Failed outcome referred to disease progression to critical illness or death. Patients who were discharged from hospital had to be quarantined for 2 weeks.

Panel 2

Definitions of clinical types of COVID-19 in paediatric patients

Mild disease

1) Upper respiratory symptoms (eg, pharyngeal congestion, sore throat, and fever) for a short duration or asymptomatic infection
2) Positive RT-PCR test for SARS-CoV-2
3) No abnormal radiographic and septic presentation

Moderate disease

1) Mild pneumonia Symptoms such as fever, cough, fatigue, headache, and myalgia.
2) No complications and manifestations related to severe conditions

Severe disease

1)Mild or moderate clinical features, plus any manifestations that suggest disease progression:
2)Rapid breath (≥70 breaths per min for infants aged <1 year; ≥50 breaths per min for children aged >1 year) Hypoxia Lack of consciousness, depression, coma, convulsions Dehydration, difficulty feeding, gastrointestinal dysfunction Myocardial injury Elevated liver enzyme Coagulation dysfunction, rhabdomyolysis, and any other manifestations suggesting injuries to vital organs

Critical illness

1) Rapid disease progression, plus any other conditions:
2) Respiratory failure with need for mechanical ventilation (eg, ARDS, persistent hypoxia that cannot be alleviated by inhalation through nasal catheters or masks)Septic shock Organ failure that needs monitoring in the ICU
3) COVID-19=coronavirus disease 2019. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. ARDS=acute respiratory distress syndrome. ICU=intensive care unit. [30]

Diagnosis kits

GenMarkDx – Multiplex Diagnostics

GenMarkDx is a Canadian company that provides multiplex molecular diagnostic test kits. Their eSensor technology is based on competitive DNA hybridization and electrochemical detection.Recently, the FDA issued Emergency Use Authorization (EUA) to the company's ePlex® SARS-CoV-2, a diagnostic test for the novel coronavirus (nCoV).

SensDx – Ultrasensitive Electrodes

Poland-based startup SensDx develops digital diagnostics solutions that enable remote healthcare. The startup uses ultra-sensitive electrodes modified with biological material to detect the presence of bacteria and viruses.

Aperiomics – Deep Metagenomic Sequencing

The US-based startup Aperiomics offers sequencing-based solutions to diagnose infections. The startup combines deep metagenomic sequencing and proprietary software, Xplore-PATHOSM, to diagnose every known bacteria, fungus, or virus in any sample, serving clinicians, patients, and researchers working on pathogens. Aperiomics has also developed a diagnostic test, Xplore-COVID-19 (PDF), to tackle the spread of the coronavirus pandemic.

MiRXES – MicroRNA Diagnostics

MiRXES is a Singapore-based startup developing microRNA biomarkers for diagnostics application. The solution combines microRNA-specific reverse transcription (RT) primers and nested quantitative PCR primer pairs to provide unparalleled specificity and sensitivity in their test.[31]

PRECAUTIONS

A. INFECTION CONTROL

- Avoid standing persons coughing and sneezing continuosly.
- Avoid shaking hands with infected persons.[32]

B. PREVENTIVE MEASURES

- Regular hand washing
- During coughing and sneezing, cover mouth and nose.
- Eat Properly cooked meat and eggs.
- Avoid contact from the person showing symptoms of respiratory illness.
- Do proper rest and avoid overexertion.
- Drink enough water.
- Avoid smoking and smoky areas.
- Take medicine to reduce pain and fever.
- Use a clean humidifier or cool mist vaporizer.[32]

THERAPEUTIC STRATERGY DEVELOPED TILL DATE

A. Allopathy treatment

B. Ayurvedic Treatment

C. Herbal Treatment

A. Allopathy treatment

i)Antivirals

Nucleoside analog Ribavirin, a nucleoside analog, shows antiviral activity against some animal CoVs, and in the SARS-CoV epidemic, many patients were treated with ribavirin along with corticosteroids and became a standard regimen for the treatment of SARS-CoV.[33]

ii)Neuraminidase inhibitors

Neuraminidase inhibitors are indicated in the management of influenza.[34] In a study on possible MERS-CoV cases in Paris from 2013 to 2016, a total of 35 patients received oseltamivir (37.6%). In patients positive for influenza virus (n = 25), 52% (n = 13) received oseltamivir and it was concluded that empirical oseltamivir can be started in suspected MERS-CoV cases.[35] Many other studies also evaluated oseltamivir in MERS-CoV. Oseltamivir was also used in the management of 2019-nCoV; however, definite evidence of efficacy is inconclusive because of lack of suitable control group in the studies.[36]

iii)Protease inhibitor

There are two types of protease present in SARS-CoV, the CL-like protease and the papain-like protease, which is important for cleaving the polyproteins and releasing the nonstructural proteins (NSP1–16), which carry out important functions in the CoV life cycle. Among protease inhibitors, lopinavir was the most inhibitor and saquinavir was the least powerful inhibitor of CoV protease.[37] In molecular dynamic studies, flap closing was observed when these inhibitors bound to the SARS-CoV3CL(pro).[38]Hong Kong University researchers demonstrated anti-SARS-CoV action of lopinavir at concentration of 4 µg/ml in vitro against the HKU-39849 isolate.[39]

Immunomodulators

i) Corticosteroids

Corticosteroids were widely used for the treatment of SERS‑CoV and MERS‑CoV and are also used in the management of the current epidemic of 2019‑nCoV.However, the interim guidelines by the WHO prohibitthe use of routine corticosteroids unless indicatedfor other clinical ground.[40]

ii) Interferon

Interferons (IFNs) are broad‑spectrum antivirals,primarily used in the treatment of hepatitis B. InSARS‑CoV patients, compared to ribavirin or interferon(IFN) alone, the benefit was seen on IFN‑α + high‑dosecorticosteroid group.[41] Other observational studies also support thesefindings and the combined useof IFN‑α and corticosteroid (corticosteroid armn = 13; corticosteroid + IFN‑α arm n = 9) showed lessdisease‑associated oxygen saturation impairment.[42] For the treatment of 2019‑nCoV.[43] IFN‑α (5 millionU bid inh) is recommended along with lopinavir + ritonavir combination.[44]

iii) Immunoglobulin

In case of critically ill SARS, who show signs of deterioration, further escalation of Immunomodulation is indicated and intravenous (i.v.) immunoglobulin may be considered.[45]

Recent Advances in the Treatment of 2019-Novel Coronavirus

Remdesivir and Chloroquine &Other Drug Combination Therapy

1. Chloroquine, which has potent antiviral activity against the SARS-CoV.[46] has been shown to have similar activity against HCoV-229E in cultured cells.[47] and against HCoV-OC43 both in cultured cells and in a mouse model.[48] However, there have been no studies of efficacy in humans.

2. Success of remdesivir in several animal models of MERS-CoV infection may lay the foundation for treatment of severe cases of COVID-19.[49]

3. The efficacy of various disinfectants was examined both on viruses in liquid suspension and on viruses dried on surfaces.[50] Human coronaviruses, including CoV-229E and SARS-CoV, as well as several animal coronaviruses (eg, mouse hepatitis virus and transmissible gastroenteritis virus of pigs), were studied. These viruses (both in suspension and dried on surfaces) were very susceptible to 70% ethanol, with reduction of viability by greater than 3 log within seconds.[51-53]

Likewise, hexachlorophene[54], 2% glutaraldehyde[53] and 1% povidone-iodine [51,53] each produced satisfactory killing. It appears that susceptibility of coronaviruses to 6% sodium hypochlorite (the active agent in bleach) solutions has been variable, but satisfactory killing was achieved with concentrations of 1:40 or higher.[51,52] Coronaviruses were not killed by benzalkonium chloride or chlorhexidine unless 70% ethanol was added.[53]

4. Combination of Antimalarial Cloroquine and Anti-swineflu Tamiflu.

B. Ayurvedic Treatment

1. The deadly coronavirus can be cured with cow dung and urine . Gomutra is effective in blood pressure, constipation and even cancer. However, when it comes to coronavirus prevention.

2. Ayurvedic herb giloy (Tinospora Cordifolia) is useful .Giloy needs to be boiled in water and then turmeric, pepper powder and tulsi leaves should be added. The mixture should then be consumed in the form of thick juice.[55]

C. Herbal Treatment

- The liquid extract from Honeysuckle and Flowering plants are stated by Chinese doctors to heal the coronavirus.
- If you are struggling with a sore throat (one of the coronavirus symptoms) then consume Lemon tea daily as it is rich in vitamin c and contains antioxidant properties.
- Staying hydrated all the time is very essential especially when you are sick. Have plenty of Fluids as this aid us to throw out the toxic materials.
- Garlic is nature available antibacterial and antiviral agent that is very beneficial to kick out illness causing enzymes.
- Frequent Gargling with hot water clears the blocked throat and allows you to intake food.
- Stuffy nosed people must prefer to have Hot water bath as this bathing aid you to soothe the nasal cavity as well as relaxes tensions and improve the quality of sleep.
- Lavender oil is one of the cheaply available essential oils that actively handles the cold and cough problems. Inhale this oil very often for quicker relaxation.[56]

CONCLUSION

To date,there is a lot known about COVI-19 .But there are several areas of research regarding the treatment of viral infection .The present review article can guide about transmission of viral infection and the methods to prevent and treat it .Understanding of the pathogenesis may eventually lead to simple,non-hazardous treatment that can be used with acute respiratory infections not only in hospitals ,but also at home to cure common colds.

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