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EC PHARMACOLOGY AND TOXICOLOGY

Review Article

COVID-19: An Overview on Transmission, Diagnosis, Co-Morbidities and Treatment

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Received: March 10, 2021; **Published:** April 29, 2021

Abstract

The current coronavirus is a highly transmittable and pathogenic viral infection triggered by severe acute respiratory syndrome coronavirus-2, which arisen in the city of China named Wuhan and had spread around the world and was declared a pandemic by World Health Organization on 11 March, 2020. COVID-19 frequently brings mild respiratory indications; it has also been displayed a capability to cause severe sickness in people who are suffering with other diseases. Reports suggested that person-to-person transmission is a common route for spreading COVID-19 infection which occurs via either direct contact or through air droplets, contaminated hands or surfaces. It was proved lethal in kids, diabetics, patients suffering from cancer or cardiovascular ailments etc. RT-PCR and CT imaging technologies was proved the best to diagnose this respiratory infection, although some other techniques are also underway like gold nanoparticles based lateral flow assay, lanthanide doped nanoparticles based lateral flow assay, field effect transistor based biosensor. Various health care professionals and scientist are working on repurposing drug approach via docking protocol. Literature reports suggested that chloroquine/hydroxychloroquine, lopinavir, ritonavir, favipiravir, Teicoplanin, auranofin, phytochemicals or traditional medicines, remdesivir showed satisfactory outcome. Various vaccines and small molecules are also under clinical trial.

Keywords: *COVID-19; Coronavirus; Co-morbidities; RT-PCR; Drug Repurposing; Ritonavir; Remdesivir; Hydroxychloroquine*

Introduction

At the end of December 2019, few cases of pneumonia were recognized in the Wuhan city of China. Wuhan is a central city of China with large population. Subsequent reports recommended that community transmission had occurred in Wuhan and Hubei province, leading to the lockdown of Wuhan on Jan 23, 2020, and subsequently other cities in Hubei province, to control the transmission of COVID-19. The epidemic's route showed a rapid upsurge globally within a few weeks and covered almost all countries. The pathogen of this viral infection was collected from throat swab. The nomenclature of this viral infection was given by the World Health Organization and declared it a pandemic on 11 March 2020 [1]. A good verdict about it was most infected individuals do not progress into severe infection and patients come out to be recovering with little to no medical interference. People suffering with other ailments were more prone to develop severe symptoms. Government found the only way to control disease is awareness about virus and its spread. Based on the data, the virus would not be painstaking a major threat to public health like the influenza virus [2]. The health professionals and government worked promptly to isolate and treat patient and enhance the process of contact tracing. The impact of pandemic was associated with social ramifications, which impacted the travel industry badly, and decelerated the global economy [3].

Coronaviruses, are members of the *Coronaviridae* family, are considered an enveloped pathogen having 27-32 kb RNA in size. Coronaviruses are single-stranded RNA viruses. This pathogen is widespread in various mammals including humans and is responsible for different other ailments [4]. In total, seven variants of Human corona viruses (HCoVs) were identified in literature. Most of the strains exhibited moderate to severe respiratory complications including SARS and MERS [5]. The COVID-19 has 14 binding dregs connected with human ACE-2. Exact working of COVID19 is not known but computational or bioinformatics scientist tried to develop its genome crystal structure that is responsible to develop severe pneumonia symptoms [6].

Transmission and prevention of COVID-19

People travelled to China were found COVID-19 active cases in a big number comparatively at the beginning of the month of February 2020 and decreases in the mid of the month. Experimental finding proved the 88% similarity of this deadly virus with the coronavirus present in the bat species which indicate a connection between human and virus. Literature data proved that virus is capable to spread its transmission from one person to another and amongst family members very rapidly. Mode of transmission in human is *via* direct touching or through respiratory drops. The higher jeopardy of transmission was within approximately 1 meter from the infected person [7]. Symptomatic cases have most infectious form of viruses although asymptomatic transmission was also observed upto incubation period i.e. between 2-10 days which lasts at maximum 14 days. Various factors like age, strength of immunity affects the incubation period and appearance of symptoms. Youngers has long incubation period compare to older generation. The common signs of this deadly virus are same like seasonal flu including cough, high temperature, fatigue, headache, weakness and severe signs are difficulty in breathing, loss of taste and smell, diarrhoea and lymphopenia. So, feacal and urine test is also recommended to trace the spread of disease and to find effective treatment [8,9]. Policymakers suggested few measured like travel restriction to containment zones, avoid contacting with symptomatic persons and surfaces and eating of meat from COVID-19 epidemic areas. Its hard to define contacts but government suggested to take maximum precautions like: (1) Social distancing (2) avoid sharing of any material with family infected person and isolate the patient in separate room (3) Use of PPE during emergency travel. Use of face masks, frequent hand washing and sanitization of surfaces, luggage's and hands should be included in routine practice. Various software and artificial intelligent technologies were also launched to provide information about the spread of infection and for necessary precautions [10]. PPE like gloves, face shield, gowns are most preferred wearable to reduce the active contact with virus. Mask is very vital component which filter the viral particulate and prevent the spread of infection. Disposable masks which prevent the transmission of contaminants from patient to wearer are preferred by healthcare professionals. Although they are unable to filter very small particles so does not provide full protection from contaminants. To overcome this problem, respirators are preferred. A big range of respirators like N95, FFP2 and 3 are available which are very efficient to filtrate very small (upto micrometer) size of contaminants [11]. Steinmann., *et al*. summarized the persistence of various correlated viruses like MERS, SARS, TGEV, MHV and human corona virus (HCoV) on different surfaces based on reports published by many scientist [12]. It was found that HCoV-229E survive for long time at room temperature than in humid environment. Persistence of human coronavirus on various surfaces at specific temperature is summarized in table 1.

Type of surface	Strain/Isolate	Temperature	Persistence
Steal	Strain 229E	21°C	5d
Aluminium	Strains 229E and OC43	21°C	2-8h
Glass	Strain 229E	21°C	5d
Plastic	Strain 229E	RT	2-6d
PVC	Strain 229E	21°C	5d
Silicon rubber	Strain 229E	21°C	5d
Surgical glove (latex)	Strains 229E and OC43	21°C	< 8h
Ceramic	Strain 229E	21°C	5d
Teflon	Strain 229E	21°C	5d

Table 1*: Persistence of human corona virus (HCoV) on different surfaces.*

#: RT= Room Temperature; d= Days; h= Hours.

Various biocidal substances like H_2O_2, ROH, NaOCl and benzalkonium type surfactants were employed for disinfection of deadly coronaviruses at varied concentrations. Sodium hypochlorite is more potent than hydrogen peroxide and effective in very low concentration comparatively. Data received with benzalkonium chloride at logical contact times were conflicting at higher concentration while ethanol was quite effective around 70%V/V strength within short span of time [13].

Cytokine storm in COVID-19

As per initial literature report, approximate 20% patients died from ARDS. ARDS was accountable immunopathological episode for coronavirus infections by cytokine storm, the fatal abandoned inflammatory reaction that evolve the huge number of pro-inflammatory cytokines and chemokine. The cytokine storm was able to produce ARDS by attacking on immune system which results in organ system failure and finally death [14].

Risk factors/co-morbidities of disease

Literature data suggested that people suffering from other serious illnesses are more vulnerable for infection. Chen., *et al*. reported that 50.5% of patients found with serious heart diseases [15]. He found that 54.3% cases were male with an average age of 56 years. Older patients with underlying illnesses required more intensive care support and observed with serious symptoms like difficulty in breathing, weakness, stomach pain, and anorexia [16]. In this section, we will summarize different reports on clinical characteristics of coronavirus in patients including children, infants, gender discrimination, imported person, pregnant woman and patient associated with diabetes, cardiovascular disease and cancer.

Clinical characteristics in infants, newborn and children

Initially, Pediatric cases were found within family member and first infant with serious infection was reported in Shenzhen in the month of January 2020. Pediatric clinical manifestations were not typical, and comparatively milder than adult patients. Infant cases were found with mild respiratory and GIT symptoms. Intrauterine transmission of infection was not observed from mother to child but close contact with mother can transmit infection. But now it was suggested to give more defensive consideration to child's and infants due to their weak immunity. The diagnosis symptoms of infants and children are also found like high fever, shortness of breath, difficulty in feeding, abnormal chest scan and confirmed test of belongings. It was also proved that children are also capable to transmit infection [17].

Active smoking and severity of COVID-19

After reviewing published literature, it was observed that only 20% cases were significantly associated with active smoking. Further study demonstrated that active smoking were also not directly correlated with the severity of infection and not associated significantly [18].

Clinical characteristics in pregnant woman

World Health Organization pointed out that hindered umbilical cord holding is suspicious for infection thatby recommended to remove after a day from birth of child. Breastmilk was found free of pathogen although infection can be transmitted through infected mother via droplets [19]. Particularly, pregnant women are more susceptible to COVID-19 due to more vulnerability to respiratory infections. Reported literature of pregnant woman suggested that patients have few diagnostic symptoms only and weigh of newborn were found lower comparatively. 60% of pregnant women delivered premature baby with other complications. All the newborns were tested negative for COVID-19 but maternal infection can affect the overall development of embryo. General attitude regarding management of COVID-19 involves early isolation, aggressive infection control procedures, testing for infection and co-infection, oxygen therapy, fetal and uterine

narrowing monitoring, mechanical ventilation for dyspnea, individualized delivery scheduling, and a collaborative method with multi-specialty consultations [20].

Clinical characteristics in diabetics

Literature data concluded that around 6 - 20% coronavirus cases found diabetics. Due to weak immunity, they are more vulnerable to develop serious symptoms and affect other organs. These patients require emergency medical attention and hospitalization. Infected patients with deadly COVID-19 with diabetes have significant impact to alter the level of glucose lowering hormones and catecholamines which worsen the diabetes complications, so routine monitoring of blood glucose of these patients is highly recommended. Considering age and other underlying disease of these patients, special clinical approaches and treatment options are required to modify to control the morbidity. Short and long-term follow-up was also requisite for diabetic patients to trim down diabetes-related complications and finally death [21].

Clinical characteristics in patients with cardiovascular complications

People with underlying cardiovascular ailment are among the highest risk persons for severe disease and fatality. Lippi and co-workers performed a study of the reported data to scrutinize the effect of troponinI (cTnI) and troponin T (cTnT) to develop serious symptoms in COVID-19 patients. He utilized the combinatorial statistical strategy using the Australia based software named MetaXL. Monitoring of level of damage of cardiac biomarkers at different intervals was studied using the statistical parameters. It was found that high damage of these biomarkers was associated with serious clinical symptoms and cardiac arrest that lead to death [22].

Clinical characteristics in cancer patients

Cancer patients are more vulnerable to COVID-19 infection due to their very weak immunity. Most of the cancer patients experienced either chemo or radiotherapy which affects their immunity significantly and they become prone for any infection. In a study of 18 patients in china, Lung cancer was the most prevalent in coronavirus patients. Older patient with cancer were more vulnerable to develop serious symptoms and require emergency medical attention. A statistical analysis of cancer patients with COVID-19 infection was performed using Cox regression approach to estimate the development of serious symptoms and rate of morbidity and found significant relation. The biggest challenge of cancer patients or any underlying disease with COVID-19 patients was to receive any medical facility because health-care sector was overloaded in this pandemic duration, although most of the healthcare professionals started online consultation for their patients. Different strategies were proposed for cancer patients with COVID-19 emergency like postponing of surgery for stable cancer, use of protective equipment's and intensive care for serious cancer patients having underlying other complications [23].

COVID-19 susceptibility in ABO blood group people

Landsteiner's ABO blood group types are basically carbohydrate epitopes exist on the cell surface. The antigenic elements of A and B groups are GalNAcα1-3-(Fucα1,2)-Galβ- and Galα1-3-(Fucα1,2)-Galβ-, while O group is Fucα1,2-Galβ. Literature data suggested that people of blood group O were less prone for infection comparatively. Yang and Wang found the COVID-19 susceptibility with ABO blood group. To understand this connection, they collected the patient's sample from different hospitals. Statistical study was accomplished using chi-squared test and using combinatorial softwares like STATA and SPSS. Results concluded that the ratio of infected person with blood group O was significantly less that other blood group patients as well as normal people and all the obtained result was validated. These studies demonstrated that the ABO blood type can provide a biomarker for differential vulnerability of COVID-19. ABO blood group spreading was also analyzed with the difference of age and sex. Statistical data concluded that blood group typing have no significant impact on age and sex of the infected patient for COVID-19. Lower prognosis for coronavirus infection of blood group O was proved by nucleic acid order resemblance and binding affinity with ACE2 [24].

Gender effect on COVID-19 severity

The COVID-19 has impacted psychological behavior of humanity like other pandemic and develop the symptoms of PTSS including anxiety, fear, stress, emotional freezing and persistent trauma. The psychological impact analysis of COVID-19 was conducted in Wuhan and other endemic cities of infection and assessed by the PTSD checklist for DSM-5 (PCL-5). The PCL-5 is a tool to measure the symptoms on five point scale comprising the different 20 parameters. Sleep pattern of patients was also evaluated using Pittsburgh Sleep Quality Index (PSQI) containing nine questions and four different parameters. Results showed that higher symptom prevalence like cognition and hyper-arousal instituted in females than males [25].

Diagnosis techniques of COVID-19

Clinical diagnosis of infected COVID-19 is mainly founded on epidemiological record, clinical expressions and some additional investigations like nucleic acid detection, CT scan, ELISA and blood culture techniques. However, the medical symptoms of COVID-19 found very atypical including difficulty in breathing, cough, high temperature and weakness. Thus, secondary examinations are required for the correct diagnosis of COVID-19. Few secondary diagnosis techniques developed and underdeveloped are summarized in this section.

Nucleic acid detection technology and CT imaging

The two commonly used nucleic acid detection technologies for COVID-19 are RT-qPCR and HTS. The reliable tool is virus blood culture and HTS of genome. However, use of HTS has several limitations like high cost and need of sophisticated instruments. So, the real-time reverse transcriptase polymerase chain reaction (RT-PCR) magnification technique is widely accepted and reflected as the "gold standard" although sometimes it can also provide false result. If RT-PCR is false negative in infected patient then CT scan played a vital role for the determination of suspected viral infection. Various literature studies on CT scanning concluded that ground glass opacity increased significantly with the rate of infection and proved it characteristic to determine the amount and severity of infection with COVID-19. However some false negative or positive results are possible here also so mutual verification of RT-PCR and CT scan is warranted for confirmatory diagnosis [26]. The CT scanning geographies of COVID-19 infection were found very nonspecific which increased the requirement of high sensitive RT-qPCR tools. However chest CT scan have some advantages like reliable, fast, and assessment of severity of infection are possible in improved way comparatively. The chest CT scanning topographies of children with coronavirus infection were non-specific although clinical signs were helpful for the effective screening. Considering the various limitations of these techniques, now immunological identification kits were introduced by various diagnosis laboratories. Considering the high demand of immuno-antibody based kit, various coronavirus N-based IgG and S-based IgG kit were developed and validated and found significant impact in early and fast detection of infection. However, sensitivity of these kits requires further research to obtain significant data [27].

Gold nanoparticles based lateral flow assay

A fast and sensitive diagnosis tool for COVID-19 is required considering the overburden on hospitals and to control the spread of infection. Based on limited resources in rural area, various challenges like testing culture, data analysis, and sample storage equipment's were faced by healthcare professionals. However, immuno-antibody based culture technique found significant and can be detected even after few days to infection. Development of IgM based kit offer significant advantages in diagnosis due to long life of this antibody in blood. Jiao and co-workers developed the gold nanoparticles based lateral flow assay for detecting IgM antibodies. Due to cost effective and operational simplicity, the technique offers several benefits for fast detection of infection. The AuNP-LF technique is much better than other similar nano-particle tools in terms of cost, use of sophisticated instrument and operational simplicity and utilizes gold nanoparticles of colloidal size. AuNPs exhibited excellent biocompatibility and lesser biological toxicity. The technique was very well tested and validated using various concentration and compared with infected samples and found significant with 1.2 mg/mL SARS-CoV-2 NP. Compared with

the RT-PCR method, the AuNP-LF assay exhibited numerous superiorities including quick test time, less sample requirement, cost effective, easy operation and independence of professional person [28].

Lanthanide doped nanoparticles based lateral flow assay

The LNPs (Lanthanide nanoparticles) were synthesized by mini emulsion polymerization strategy and tested with IgG antibody of human and rabbit for the further development of test strip for the diagnosis of deadly coronavirus. The assay was not improved from semi-quantitative to accurate quantification due to unavailability of official anti-SARS-CoV-2 IgG reference. However, the outcome of the validation experiment meets the necessities for clinical diagnostic reagent [29].

Field-effect transistor-based biosensor

A very high sensitive technique named "field-effect transistor (FET)-based biosensing" was developed and used for various, clinical diagnosis and on-site fast detection of coronavirus infection by using the very small amount of sample. Collaborated efforts of Park and Kim group's reported a graphene-based device for detection of SARS-CoV-2 infection. This highly sensitive and rapid device is based on the collection of sample from nasal swab and their culture and limit of detection was found to 1.0 fg/ml [30].

Treatment possibilities

Any specific medication was not developed yet for the specific treatment of COVID-19. Symptomatic relief was ascertained by the use of paracetamol, oxygenation technique and few medicines like antibiotics, Ivermectin and CQ/HCQ. Severely affected patients require emergency facility like high flow oxygen therapy and recovering plasma therapy and possible ventilation. The only treatment alternative available is broad-spectrum antivirals like nucleoside analogues and HIV-protease inhibitors that could lessen virus infection until the specific antiviral drug becomes available. Clinically, aerosol management of alpha-interferon, lopinavir/ritonavir, ribavirin were also tried and showed beneficial effect to reduce symptoms although use of more than two drugs was not suggested [31]. Various other drugs for infection like influenza are under clinical trial like EIDD-2801 using the approach of drug repurposing [32]. Initially in Shanghai, doctors tried the plasma therapy. In this technique, plasma was isolated from recovered coronavirus patients and vaccinated in the infected patients and observed amazing results. The same process was also followed in other countries to treat severe cases with prior approval of government. The process is termed plasma therapy [33]. In this section, we will discuss various drugs or probable treatment option under clinical trials.

Docking study for drug repurposing

Considering the current epidemic situation, it would be extremely valuable to repurpose old drugs for clinical treatment. Various literature reports suggested that SARS-CoV-1 3CLpro enzyme is required in the life cycle of coronavirus that's by targeting this enzyme is hope to develop anti-COVID drug. Various anti-HIV drugs inhibit this enzyme and open the way of drug repurposing. Yang and co-workers extracted crystal structures of 3CLpro-2 and 3CLpro-1 from the Protein Data Bank and docked with six protease inhibitors like lopinavir, ritonavir, indinavir, saquinavir, darunavir, tipranavir using the concept of drug receptor binding and calculated docking energy which was found lowest for indinavir and darunavir showing the highest affinity for 3CLpro-2. 3CLpro is vital for corona virus duplication and its inhibition has potential to develop new drugs for the treatment of COVID-19 infection [34]. Elfiky and co-workers performed the docking study of eight compounds using the optimized COVID-19 and SARS RdRps using AutoDock Vina. The selected compounds like sofosbuvir, ribavirin, remdesivir, cinnamaldehyde and thymoquinone already has strong potential against a variety of viral infections including coronavirus. Results concluded the significant output as they inhibited RdRp effectively and found superior potency [35]. Owis., *et al*. designed the efficacy of medicinal plant-based bioactive compounds, isolated from *S. persica* against COVID-19 using computational study employing the darunavir as reference drug. Compounds for study were identified from the aqueous fraction of *S. persica* aerial parts using

LCHRESIMS for dereplication purposes. Detection of chemically related flavonoids enabled to check the connection between structure and receptor interactions in the N3 binding site of COVID-19 protease. Docking results found that flavonoid compounds were better fit than darunavir [36].

4-aminoquinolines against COVID-19

4-aminoquinolines is a class of aminoquinoline where -NH_2 group present at the 4-position of the quinoline. Quinoline has wide pharmacological spectrum including malaria and virus. The prototype compound of this class initially isolated from cinchona bark. Examples include chloroquine, hydroxy chloroquine, amodiaquine etc. Apart from malaria, quinoline derivatives have reported for broad spectrum of pharmacological effects like anti-asthmatic, antibacterial, anti-fungal, anti-malarial, antiviral and anti-inflammatory. During the COVID-19 pandemic, Chinese scientist found the efficacy of chloroquine phosphate against COVID-19. Chloroquine acts by multiple mechanisms which are well proved in literature. Literature reports suggested that chloroquine exhibit activity against coronavirus by the glycosylation of the cellular receptors. Reported literature suggested that both chloroquine and remdesivir has *in vitro* COVID-19 activity. Hydroxychloroquine is also congener of chloroquine which is administered orally. Retinopathy is a critical side effect of hydroxychloroquine above the dose of 6.5 mg/kg body weight. Due to low safety margin, chloroquine and hydroxychloroquine use should be subjected to strict rules and with the supervision of medical practitioner only. Some precautions will be required like frequent monitoring of RBC, WBC and platelet counts, functioning of hepatic and renal system and blood glucose monitoring. Drugs which extend QTc interval are generally contra-indicated with chloroquine and HCQ due to its synergistic effect on cardiovascular system and ECG monitoring is required. Chloroquine was found safe during pregnancy [37,38].

Lopinavir and ritonavir

Ritonavir is a protease inhibitor, it is generally used to inhibit cytochrome P450 3A4 and strikingly increases the plasma concentrations of other protease inhibitors. However, it is under dispute whether HIV protease inhibitors could effectively target the SARS-CoV-2 3CLpro. This is based on the piece of evidence that HIV protease is from the aspartic protease family, whereas the SARS-CoV-2 $3CL^{pro}$ belongs to the cysteine protease family. Rungrotmongkol and Co-workers investigated the binding interactions of lopinavir and ritonavir towards the SARS-CoV-2 protease by molecular modelling and quantum chemical methods. According to ΔG_{bind} prediction, the propensity against the SARS-CoV-2 $3CL^{pro}$ of ritonavir was higher than Lopinavir. The study was supported by energy stabilization from individual residues [39]. Dayer., *et al*. performed *in silico* study of HIV-1 protease inhibitors with Mpro to understand the mechanism for possible drugs for coronavirus infection. In his protocol, the best enzyme-inhibitors complex with maximum binding energy were selected for MD simulations and subsequently serial docking experiment was conducted in triplicate to pull out favourite binding site and found Lopinavir as highest potent. Zhang and co-workers conducted a study on deadly coronavirus patients to find the clinical potency of Lopinavir employing ten patients in his study. He found approximate 70% efficacy of this drug although eosinophil value were low at initial stage which was recovered after relieving from infection. The use of lopinavir appears to be effective but digestive adverse effects and hypokalemia were observed by clinicians [40].

Favipiravir

It is a novel RNA-dependent RNA polymerase (RdRp) inhibitor, which has been revealed to be effective in the treatment of influenza and Ebola virus. It is pyrazine carboxamide derivatives widely studied for various viral infections. It is a prodrug of favipiravir-ribofuranosyl-5'-triphosphate (favipiravir-RTP) and approved for clinical trial against the deadly coronavirus infection. Due to disaster of COVID-19, favipiravir was approved for sale in February 2020 in China. Reports from clinical trials of favipiravir against COVID-19 were published by the Ministry of Science and Technology of the People's Republic of China at a COVID-19 themed press conference. Zhong and Liu conducted an open-label nonrandomized control study in the isolation ward of the national clinical research centre for infectious diseases, China. Patients who had initially been treated with lopinavir/ritonavir from 24 January to 30 January 2020 were screened, and eligible

patients were incorporated in the control arm of the study. It was observed that favipiravir was independently coupled with quicker viral clearance in chest imaging. The results suggested that favipiravir has significantly better effects on COVID-19 patients compared to lopinavir/ritonavir [41].

Teicoplanin

Teicoplanin, an effective antibiotic against *Staphylococcal* infection has proved to exhibit potency against various viral infections including SARS and MERS, also found the *in vitro* activity against COVID-19. Zhou and colleagues explored the mechanism of teicoplanin and concluded that it interfere with the virus life cycle by chopping spike protein by cathepsin L [42].

Metal based drug/auranofin

Auranofin was initially discovered for the treatment of rheumatoid arthritis but now its in the clinical trial for viral diseases. Auranofin has shown a tolerable toxicity profile and was proved safe for human use. Reported data concluded that it also exhibited potential against HIV infection and was proved better than chloroquine and hydroxychloroquine. Auranofin was proved to hamper the JAK1 and STAT3 to obstruct cysteine proteases. Kumar and co-workers reported that Auranofin strongly inhibits SARS-COV-2 replication at a low micro molar concentration in human cells with 95% reduction of viral RNA. Auranofin was also originated to spectacularly diminish the expression of SARSCOV-2-induced cytokines in human cells [43].

Natural product derived phytochemicals

Traditional medicines have long history and played a vital role in the prevention and treatment of several pandemic including for diagnosis and treatment of viral infection. Various Chinese natural products were used to cure the infection of deadly coronaviruses like *gancaoganjiang* decoction, *qingfeitouxie fuzheng recipe*, *Glycyrrhizae Radix, Gypsum Fibrosum, Cinnamomi Ramulus, Alismatis Rhizoma, Poria, Bupleuri Radix, Scutellariae Radix, Zingiberis Rhizoma Recens, FarfaraeFlos, Belamcandae Rhizoma, Dioscoreae Rhizoma, Aurantii Fructus Immaturus, and Pogostemonis Herba*. Runfeng and co-workers highlighted the necessity to isolate and synthesized the natural product based potent and effective molecules having diverse pharmacological potential. Chinese herbal product *Lianhuaqingwen* exhibited wonderful activity for COVID-19 and compared with remdesivir. Polyphenols also demonstrated antiviral activity like quercetin showed an IC50 of 8.6 ± 3.2 μM against SARS-CoV PLpro. Various plant lectins were evaluated for their antiviral activity and found potential candidate against a broad range of viruses. Various other herbal products like *Strobilanthes cusia* and *Sambucus Formosana* also showed specific potential against the selective strain of coronavirus like HCoV-NL63 in dose dependent way and found highly efficacious. With further extensive investigation of the phenolic symphony of the extracts, caffeic acid was recognized as the most potent compound (EC50 of 3.54±0.77 μM; or ~0.64±0.14μg/mL) [44].

High flow oxygenation assisted tracheal intubation

Li and Cao., *et al.* evaluated the efficacy and safety of high-flow nasal oxygenation (HFNO) and standard mask oxygenation (SMO) in coronavirus severe adult patient facing hypoxia issue and required emergency treatment and found that the HFNO is better technique comparatively. The technique is significantly capable to increase the air capacity of lungs by positive pressure although do not work in case of bacterial contamination in lungs. Overall, High-flow nasal oxygenation was proved potentially constructive during rapid-sequence induction and intubation in severe COVID-19 patients [45].

Recent research and development on drugs and vaccines for COVID-19 and related HCV

Target identification and validation is critical challenge for development of either new drugs or repurposed drugs for the effective and safe treatment of coronaviruses. Based on the knowledge of discovery of other antiviral drugs like Lopinavir and ritonavir and remdesi-

vir, scientist had to think that proteases like 3CLpro and PLpro and RdRp polymerases might be amazing targets for the anti-COVID-19 discovery and clinical trial for these drugs are under progress. Not only existing drugs, but several new chemical entities are also under development which has shown its potency against similar pathogens. Scientist are also working in the area of drug repurposing using the in-silico approach to reduce the time for effective drug discovery for the possible treatment of COVID-19. Biologics and vaccines are potential candidates to develop immunity in the host cell. Fortunately, various vaccines were launched by different multinational pharma companies with the association of research organizations and government. Currently few vaccines like Covishield, Covaxin, Sputnik and BioNTech are available and various other vaccines are expected to come soon [46].

Role of diet

The role of diet and nutrition are critical to reduce the impact of the COVID-19 virus on the severity of the disease. Dietary activators that activate anti-aging genes in diabetes, cardiovascular disease and other diseases are important to prevent the severity of the COVID-19 infection. In the developing world the severity of the COVID-19 virus may be improved by improvements in food quality and a reduction in the xenobiotic toxicity. Drug therapy that need to be used in COVID-19 may require intact and rapid hepatic drug metabolism in these infected individuals [47-50].

Conclusion

Based on our interest on pharmacology, drug development and medicinal chemistry [51-71], we summarized the prevention, diagnosis, co-morbidities and treatment possibilities of COVID-19 in this review article. This review provides broad information about COVID-19. For diagnosis of infection, RT-PCR or combined approach should be adopted. Government of every country suggested adopting precautionary measures like social distancing, isolation and use of protective equipments like face-mask, sanitized and face-shield etc to prevent the transmission of this pandemic until any specific drug will not be discovered. It was pointed out that patients with underlying health issues like diabetes, cancer, cardiovascular ailments, and respiratory diseases are more vulnerable for infection. Researchers found drug repurposing approach to identify potent drug in short span of time although various small molecules, phytochemicals, other antiviral and vaccines are under clinical trial, although four vaccines are currently available in global market. Various drugs such as chloroquine/hydroxychloroquine, lopinavir, ritonavir, favipiravir, Teicoplanin, auranofin, phytochemicals or traditional medicines, remdesivir showed satisfactory outcome.

Acknowledgements

We acknowledge the faculty members and management of SVKM's NMIMS, University for their guidance and support.

Conflict of Interest

The author confirms that there is no conflict of interest for this publication. No animal and human volunteers were used during production of this article.

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