International Journal of Research in Pharmacy and Pharmaceutical Sciences
ISSN: 2455-698X; Impact Factor: RJIF 5.22
Received: 09-02-2020; Accepted: 02-03-2020; Published: 07-03-2020
www.pharmacyjournal.in
Volume 5; Issue 2; 2020; Page No. 01-09

SARS coronavirus: A review of threat in global world

Pallavi Chandewar[1], Bhairavi Chavhan[2], Atish Sahare[3], Pooja Deshpande[4], Dinesh Kawade[5*]
[1-4] Bajiraoji Karanjekar College of Pharmacy, Sakoli, Distt Bhandara, Maharashtra, India
[5] Priyadarshini JL College of Pharmacy, Electronic Zone Building, MIDC, Hingna Road, Nagpur, Maharashtra, India

Abstract
The coronavirus the cause of an outbreak of respiratory illness in Wuhan, Hubei Province, China beginning in December 2019. This virus appears to be a new human pathogen to causes Severe Acute Respiratory Syndrome (SARS) and get quickly spread to all over world before it was controlled. Initially, the new virus was called 2019-nCoV. Subsequently, the task of experts of the International Committee on Taxonomy of Viruses (ICTV) termed it the SARS-CoV-2 virus. Human corona viruses most commonly spread from an infected person to others through respiratory droplets, close personal contact with an infected person or by touching an object or surface infected with the corona virus and then touching the same hand to mouth or eye. Till now, there is no approved antiviral drug or vaccine for the management of infection by coronavirus. However, from earlier experience, many therapeutic agents are being used in the treatment of SARS-CoV-2 virus. The World Health Organization announced that the outbreaks of the novel coronavirus have constituted a public health emergency of international concern. Infection control measures are necessary to prevent the virus from further spreading and to help control the epidemic situation. This article, based on available literature evidence, introduces coronavirus through its structure, pathogenesis, etiology, diagnosis, clinical features, and prevention and control and therapeutic options.

Keywords: SARS coronavirus, structure, pathogenesis, clinical features, diagnosis, therapeutic options

1. Introduction
In corona virus, the word corona represents crown-like spikes on the outer surface of the virus; thus it was named as a corona virus. These are minute in size ranging from 65-125 nm in diameter, and contain a single stranded RNA ranges in size 26-32kbs in length [1]. 36 corona viruses belongs to the family Coronaviridae within the order Nidovirales, which are responsible for causing respiratory infections or intestinal infections in the humans or animals. SAR-CoV belongs among these 36 corona viruses, responsible for severe respiratory infections [2].

There are mainly four types of genera of coronaviridae family which include Alfacoronavirus, Betacoronavirus, Deltacoronavirus and Gamacoronavirus as well as it include several subgenera and species. The variety of corona viruses are mainly found in humans and animals. There are different types of Human Coronaviruses (HCoVs) are present which include HCoV-229 and HCoV-NL63 which come under the genus alfacoronavirus, at the same time HCoV-OC43 and HCoV-HKU1 which are belongs to the subgenus Embecovirus of genus betacoronavirus. In 1960s, the human coronaviruses were firstly isolated in cell culture from person with upper respiratory infections. These were later designated as HCoV-229E and HCoV-OC43. Also in early 2000s, the HCoV-NL63 and HCoV-HKU1 were discovered from person suffering from bronchiolitis and pneumonia. Later in 2002, Severe Acute Respiratory Syndrome related coronavirus (SAR-CoV) (the name taken from severe respiratory disease) was originated from a betacoronavirus in lineage B (subgenus: Sarbecovirus) from bats and then spread through civets to human in the Guangdong province of southern china. In 2012 the name Middle East Respiratory Syndrome related coronavirus (MERS-CoV) which have similar clinical syndrome as like SARS which spread from camel to human in Saudi Arabia [3]. The mammals are mainly affected by the alpha and betacoronavirus, while gamma and deltacoronavirus infect the birds but in some cases they found to infect the mammals. The respiratory illness in humans and gastroenteritis in animals usually cause due to alfa and betacoronaviruses. In humans, the severe respiratory syndrome cause due to highly pathogenic viruses i.e. SAR-CoV and MERS-CoV and the mild upper respiratory disease in immunocompete hosts cause due to other four human coronaviruses include CoV-NL63, HCoV-229E, HCoV-OC43 and HCov-HKU1; although some of them are also responsible for severe infections in infants, young children and elderly individual [4]. World Wide, the reason of increase in fatality rate and pulmonary failure is due to highly pathogenic viruses like SAR-CoV, H5N1 influenza A, H1N1 2009 and MERS-CoV which cause acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) [1]. In China, at the end of 2019, the first fifty days were epidemic because within those days, Wuhan an emerging business hub of China experienced an outbreak of a novel coronavirus that killed more than eighteen hundred and infected over seventy thousand individuals. Initially, the researchers focused on spreadability and infectivity of virus and on that basis it was suggested that the patients suffering from coronavirus firstly induce pneumonia in China, may have visited to the seafood market where live animals were sold or may have used infected animals or birds as a source of food. However, further investigations revealed that some individuals also get infected even they were not visiting to seafood market. These observation indicated that virus have capability to spread from human to human, which was subsequently reported in more than 200 countries in the world. The activities like close contact with infected person

exposed to coughing, sneezing and respiratory droplets of infected person responsible for lung infection as they can penetrate the lungs of human via inhalation through the nose and mouth. It was reported that this virus belongs to member of β-group of coronaviruses. The Chinese researchers named this novel virus as Wuhan coronavirus or 2019-novel coronavirus (2019-nCoV). Another name for virus suggested by the international committee on Taxonomy of viruses (ICTV) is SARS-CoV-2 and the disease as COVID-19 [5].

In China, the coronavirus spread quickly within one month throughout the country during Chinese new year- a period when there is a high level of human mobility among Chinese people. Although it is still too early to predict susceptible population, early patterns have shown a trend similar to SAR-CoVs and MERS-CoVs. The age, biological sex and other health conditions are seems susceptible to viral infection. In current situation, WHO declared the COVID-19 as a Public Health Emergency of International Concern. There are many articles were published about this epidemic situation by the research community which include the spread of the new coronavirus and its impact on human health. Regarding the new coronavirus, we conducted a brief review which includes a summary and analysis of various published literature. This review aims to provide knowledge about coronavirus structure, etiology and transmission, SARS-pathogenesis, diagnosis, prevention and control and therapeutic option. The ultimate aim of present review article is to aware the community about coronavirus and its infection as well as these review study try to provide a data for curious scientific professionals who can contribute their efforts to fight such like threatening infections.

2. Structure

The different studies indicate that coronavirus virions are spherical with diameters of approximately 125 nm as depicted by cryo-electron tomography and cryo-electron microscopy. The most spectacular feature of coronaviruses is the club-shape spike projections emanating from the surface of the virion. The solar corona appearance of coronaviruses is due to these spikes which is well defining feature of the virion. Coronaviruses have helically symmetrical nucleocapsids which is present within the envelope of the virion. It is more common for negative-sense RNA viruses, but uncommon among positive-sense RNA viruses. Coronavirus particles contain four main structural proteins including spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins and these proteins are encoded within the 3′ end of the viral genome.

The heavily N-linked glycosylated S protein (~150 kDa), utilizes an N-terminal signal sequence to gain access to the ER. On the surface of the virus, the distinctive spike structure is form by the homotrimers of S protein encoded virus. The trimeric S glycoprotein is a class I fusion protein and mediates attachment to the host receptor. S is cleaved by a host cell furin-like protease into two separate polypeptides noted S1 and S2, this is occur in most but not in all coronaviruses. The large receptor-binding domain of the S protein is makes up by S1 while S2 forms the stalk of the spike molecule.

The most abundant structural protein in the virion is the M protein. It is a small (~25–30 kDa) protein with 3 transmembrane domains and is believed to give the virion its shape. The structure contains small N-terminal glycosylated ectodomain and a much larger C-terminal endodomain that extends 6–8 nm into the viral particle. Despite being co-translationally inserted in the ER membrane, most M proteins do not contain a signal sequence. The different studies suggest the M protein may adopt two different conformations allowing it to promote membrane curvature as well as bind to the nucleocapsid and it exists as a dimer in the virion.

The E protein (~8–12 kDa) is found in small quantities within the virion. E protein has a common architecture but they are highly divergent from coronaviruses. The data suggest that E protein is a transmembrane protein but the membrane topology of this is not completely resolved. The E protein has ion channel activity along with N-terminal ectodomain and a C-terminal endodomain. As opposed to other structural proteins, recombinant viruses lacking the E protein are not always lethal although this is virus type dependent. In coronavirus, the E protein facilitates assembly and release of the virus. E protein is not required for viral replication but is required for pathogenesis for the occurrence of ion channel activity in the SARS-CoV.

In the nucleocapsid the only protein present is the N protein. An N-terminal domain (NTD) and a C-terminal domain (CTD), these are the two separate domains constitute in N protein. Both domain are capable of binding RNA *in vitro*, but they have different mechanisms to bind RNA. For the optimal RNA binding, contributions of both domains is necessary. N protein is also heavily phosphorylated for enhancing the affinity for viral versus non-viral RNA by trigger a structural change with the help of phosphorylation. The binding conformation for N protein to viral genome in a beads-on-a-string type. For N protein, two specific RNA substrates have been identified; the transcriptional regulatory sequences (TRSs) and the genomic packaging signal. The genomic packaging signal has been found to bind specifically to the second, or C-terminal RNA binding domain. The N protein also bind to the key component of the replicase complex i.e. nsp3 as well as to the M protein. These protein interactions likely help tether the viral genome to the replicase-transcriptase complex (RTC), and subsequently package the encapsidated genome into viral particles.

The hemagglutinin-esterase (HE) is considered as a fifth structural protein, is present in a subset of β-coronaviruses. These protein have acetyl-esterase activity, acts as a hemagglutinin and express the binding with sialic acids on surface glycoproteins. These activities might be due to enhancement of S protein-mediated cell entry and virus spread through the mucosa [6].

3. Etiology and Transmission

The positive-stranded RNA CoVs characterized with the presence of spike glycoproteins on the envelope [7]. Generally, the bats and rodents are the gene sources of alphaCoVs and betaCoVs, as shown by Genomic characterization. On the contrary, the gene sources for deltaCoVs and gammaCoVs are seem to be avian species. The various health issues can cause due the different viruses such as respiratory, enteric, hepatic, and neurological diseases in the different animal species, including camels, cattle, cats, and bats. Till date, it is identified that there are seven human CoVs (HCoVs) capable to infect humans. In general,

estimates suggest that healthy carriers of a CoV are 2% of the population and that these viruses are responsible for causing acute respiratory infections in range of 5% to 10% of population [8].

The HCoV-OC43, HCoV-HKU1, HCoV-229E, and HCoV-NL63 are the common HCoV which can cause common colds and self-limiting upper respiratory infections in immunocompetent individuals. The lower respiratory tract infections can mainly occur in the elderly persons and in immunocompromised. The epidemics situation with variable clinical severity is mainly due to other HCoVs including SARS-CoV, SARS-CoV-2, and MERS-Co featuring respiratory and extra-respiratory manifestations. The mortality rates concerning SARS-CoV and MERS-CoV are up to 10% and 35%, respectively.

In genetic terms it get prove that the genome of the new HCoV, isolated from a cluster-patient with atypical pneumonia after visiting Wuhan, had 89% nucleotide identity with bat SARS-like-CoVZXC21 and 82% with that of human SARS-CoV. For this reason, the new virus was called SARS-CoV-2. SARS-CoV-2 is sensitive to ultraviolet rays and heat like other CoVs. Furthermore, the lipid solvents including ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform (except for chlorhexidine) can be used for effective inactivation of these viruses [9]. The 29891 nucleotides (encoding for 9860 amino acids) are present in single-stranded RNA genome of SARS-CoV-2. Although its origins are not entirely understood, these genomic analyses suggest that SARS-CoV-2 probably evolved from a strain found in bats. However, there is no idea about the potential amplifying mammalian host, intermediate between bats and humans. Since the mutation in the original strain could have directly triggered virulence towards humans, it is not certain that this intermediary exists [10].

Transmission

The animal-to-human transmission of the COVID-19 was presumed as the main mechanism, because the first case of the COVID-19 disease was linked to direct exposure to the Huanan Seafood Wholesale Market of Wuhan. Nevertheless, subsequent cases were not associated with this exposure mechanism. Therefore, it was concluded that the symptomatic people are the most frequent source of COVID-19 spread, because these virus could also be transmitted from human-to-human. The possibility of transmission before symptoms seems to be develop infrequent, although it cannot be excluded. Moreover, there are suggestions that individuals who remain asymptomatic could transmit the virus. This data suggests that the isolation is only the best way to reduce this epidemic.

The transmission is believed to occur through respiratory droplets from coughing and sneezing, and also due to other respiratory pathogens, including flu and rhinovirus. Aerosol transmission is also possible in case of protracted exposure to elevated aerosol concentrations in closed spaces. In China, analysis of data related to the spread of SARS-CoV-2 seems to indicate that there must be close contact between individuals. In fact, primarily, the spread of disease is limited to family members, other close contacts and healthcare professionals.

On the basis of investigations conducted in the China and data from the first cases in Wuhan concluded that the incubation time could be generally within 3 to 7 days and up to 2 weeks. 12.5 days was considered as the longest time from infection to symptoms [10]. This data also showed that this novel epidemic doubled about every seven days, whereas the basic reproduction number is 2.2. In other words, on average, each patient transmits the infection to an additional 2.2 individuals [11].

4. SARS Pathogenesis

In COVID-19 infected patients, they showed abnormalities like higher leukocyte numbers, respiratory findings, and increased levels of plasma pro-inflammatory cytokines. In one of the COVID-19 case reports, infected patients showed symptoms like 5 days of fever presented with a cough, coarse breathing sounds of both lungs, and a body temperature of 39.0°C. The result in positive real-time polymerase chain reaction in patient's sputum confirmed COVID-19 infection. The laboratory studies showed leucopenia with leukocyte counts of 2.91 × 10^9 cells/L of which 70.0% were neutrophils. Additionally, a value of 16.16 mg/L of blood C-reactive protein was noted which is above the normal range (0–10 mg/L). High erythrocyte sedimentation rate and D-dimer were also observed [12]. The respiratory system targeting virus which causes severe pneumonia RNAaemia, combined with the incidence of ground-glass opacities, and acute cardiac injury, were the main pathogenesis of COVID-19 infection. Significantly high blood levels of cytokines and chemokines were noted in patients with COVID-19 infection that included IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA. high levels of pro-inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα showed by some of the severe cases that were admitted to the intensive care unit, that are reasoned to promote disease severity [13].

A proposed SARS disease model was consisting of three phases: viral replication, immune hyperactivity, and pulmonary destruction. Diffuse alveolar damage, epithelial cell proliferation, and an increase of macrophages of the lung have been included in SARS pathology. The characteristic feature of many coronavirus infections are multinucleate giant-cell infiltrates of macrophage or epithelial origin have been associated with putative syncytium-like formation. The observation lymphopenia, hemophagocytosis in the lung and white-pulp atrophy of the spleen in SARS patients are reminiscent of those reported for fatal influenza virus subtype H5N1 disease in 1997. Strikingly, a cytokine deregulation is supports by the presence of hemophagocytos. SARS is considered as a viral pneumonia widely. However, the gastrointestinal symptoms, splenic atrophy and lymphadenopathy may also exhibit SARS patients. Diarrhea is a very frequent finding in SARS patients (30 to 40% of patients). In enterocytes, SARS-CoV replicates with minimal disruption of the intestinal architecture. The absence of intestinal inflammation has been speculated to be a result of upregulation of transforming growth factor β and an antiapoptotic host cellular response in the intestinal epithelial cells. SARS is a systemic disease with widespread extrapulmonary dissemination, is proposed by the recent findings which are based on autopsies of SARS patients. This condition of patients results in viral shedding in respiratory secretions, stools, urine and even sweat.

On stimulation of macrophages, proinflammatory cytokines

released in the alveoli may have a role in the pathogenesis of SARS. The SARS-CoV infection of macrophages in vitro leads to the initiation of viral replication and viral protein synthesis, but replication is abortive and no virus particles are produced. In contrast to the case for influenza-A virus and HCoV-229E, no IFN-α/β response is detected in macrophages, despite the induction of the expression of chemokines such as CXCL10/IFN-γ-inducible protein 10 and CCL2/monocyte chemotactic protein.

It has been clearly reported that replication of SARS-CoV is occur in peripheral blood mononuclear cells (PBMCs) from SARS patients. A microarray platform which includes more than 8,000 gene sequences is used for analysis of gene expression of PBMCs of SARS patients and this method suggests that the response of SARS patients seems to be an innate inflammatory response, rather than a specific immune response against a viral infection. The researcher which did not find significant upregulation of major histocompatibility complex class I genes or major cytokines, including IFNs (IFN-α, IFN-β, and IFN-γ), or genes involved in complement-mediated cytolysis, concluded that the immune response against the SARS-CoV may be different from that in other viral infections or that the virus may be using an unusual strategy to evade the host immune system and cause the pathogenesis and mortality.

The immune evasion by SARS-CoV suggests the increasing viral load and Lymphopenia in the first 10 days of SARS. In SARS-CoV-infected cells, the lack of an IFN-β response, has been in vitro reported using human primary myeloid-derived dendritic cells and the epithelial 293 cell line. It is demonstrated that by preventing the induction of IFN-β through interfering with the activation of IFN regulatory factor 3, SARS-CoV escapes interferon-mediated growth inhibition. The mechanism of lymphopenia remains unclear. By direct viral infection, it seems unlikely that SARS-CoV-induced lymphopenia occur because of the absence of ACE2 expression in T- and B-cell lymphocytes. Rather it has been suggested that these observation of the acute lymphopenia in SARS patients due to apoptosis of uninfected lymphocytes [14].

5. Clinical features

The disease may be classified into mild, moderate, severe and critical. Fever (98.6%), fatigue (69.6%), dry cough and diarrhea are the most common symptoms in COVID-19 patients. COVID-19 manifests with a wide clinical spectrum ranging from asymptomatic patients to septic shock and multiorgan dysfunction.

- **Mild Disease:** An upper respiratory tract viral infection is symptoms which may be present with mild illness in patient. These include dry cough, mild fever, nasal congestion, sore throat, headache, muscle pain and malais. It is also characterized by absence of dyspnea which is a serious symptoms. Patients with mild disease can quickly deteriorate into severe or critical cases.
- **Moderate Disease:** In these, the patients suffer with respiratory symptoms of cough, shortness of breath and tachypnea. However, there is no occurrence of any signs and symptoms of severe disease.
- **Severe Disease:** Syndrome like severe pneumonia, acute respiratory distress, sepsis, or septic shock are mainly present in patients with severe disease. Diagnosis is clinical, and complications can be excluded with the help of radiographic studies. In clinical presentations, the presence of severe dyspnea, tachypnea (respiratory rate>30/minute), respiratory distress and/or greater than 50% lung infiltrates within 24 to 48 hours are included. Even, the fever can be absent or moderate in severe forms of the disease.
- **Critical disease:** Patients can develop respiratory failure, RNAaemia, cardiac injury, septic shock, or multiple organ dysfunctions in critical disease and the percent of developing these disease in patient is 5%. As per the data from the Chinese Centers for Disease Control and Prevention (CDC), the case fatality rate for critical patients is 49%. There is high fatality rate in patients with preexisting comorbidities. However, patients without comorbidities have a lower case fatality rate (0.9%). These comorbidities include diabetes (7.3%), respiratory disease (6.5%), cardiovascular disease (10.5%), hypertension (6%) and oncological complications (5.6%).
- **Sepsis and Septic Shock:** Patients with COVID-19 and sepsis are considered to be the most critical patients. The consequence of dysregulated host response to infection result in multiorgan dysfunction. Few signs which denotes the multiorgan dysfunction include severe dyspnea, low oxygen saturation, reduced urine output, tachycardia, hypotension, cold extremities, skin mottling and altered mentation. Laboratory evidence of other homeostatic dysregulation includes acidosis, high lactate, hyperbilirubinemia, thrombocytopenia and evidence of coagulopathy. Patients with septic shock are persistently hypotensive despite volume resuscitation. They may also have an accompanying serum lactate level of >2 mmol/L [15].

6. Diagnosis

It has been reported that longer than two weeks, people can carry the virus without symptoms and cured patients discharged from hospitals can carry the virus again, which sends out for particular time to quarantine.

At the early stage, patients have normal or reduced number of peripheral white blood cells (especially lymphocytes). For example, lymphopenia with white blood cell count < 4×10^9/L including lymphocyte count < 1×10^9/L, and elevated aspartate aminotransferase levels and viremia were found in 1099 COVID-19 patients. In some patients, the levels of liver and muscle enzymes and myoglobin were increased in the blood and sedimentation of C-reactive protein and erythrocyte in the blood were also increased in most of the patients. In patients with severe cases, the lymphocyte count was progressively reduced, and the level of D-dimer, a fibrin degradation product present in the blood, was elevated [16].

Currently, to confirm the cases, real-time reverse transcription-polymerase chain reaction (rRT-PCR) based technique is used. The respiratory specimen preferably from the lower respiratory tract (sputum, bronchoalveolar lavage, bronchial aspirate) is used for higher yield. Upper respiratory specimen (nasopharyngeal) is also used to detect SARS-CoV-2. In suspected cases, a newer kit is developed to detect serum immunoglobulin which can give results in 15 minutes. In China, the chest X-ray and CT scan of the chest with characteristic findings are also included as cases. Chest X-ray showing bilateral infiltrates and in computed tomography (CT), chest ground-glass opacities are said to be characteristic. In the initial epidemic area of China, for

the diagnosis of COVID-19, the study with CT had a higher sensitivity as compared with initial reverse-transcription polymerase chain reaction (RT-PCR) from swab samples. It is observed that diagnosis of suspected patients with COVID-19, the positive rates of RT-PCR assay and chest CT imaging in the cohort were 59% (601/1014), and 88% (888/1014) respectively. With RT-PCR as a reference, the sensitivity of chest CT imaging for COVID-19 was 97% (580/601). In patients with negative RT-PCR results but positive chest CT scans (n = 308 patients), 48% (147/308) of patients were re-considered as highly likely cases, with 33% (103/308) as probable cases by a comprehensive evaluation. With the analysis of serial RT-PCR assays and CT scans, 60% to 93% of patients had initial positive chest CT consistent with COVID-19 before the initial positive RT-PCR results. The 42% of patients showed improvement of follow-up chest CT scans before the RT-PCR results in turning negative. In the USA, the presence of SARS-CoV-2 RNA in feces is identified in some cases. By checking renal function, sepsis markers and assessing the co-morbidities the extent of organ damage can be ascertained [17].

7. Prevention and Control

Presently, there are no vaccines to prevent COVID-19. Hence, avoid exposure to persons suspected or confirmed to have COVID-19 is the best way to protect against COVID-19. Some important preventive measures are as follows.

- Hands must be washed often with soap and water for at least 20 seconds, especially after going to the bathroom, before eating, when hands are visibly dirty and after blowing your nose, coughing or sneezing. If soap and water are not available, use an alcohol-based hand sanitizer containing at least 60% alcohol.
- In case of coughing and sneezing, the mouth and nose should be covered with a tissue and throw the tissue into a closed bin followed by hand hygiene. It is also advised to cough into the bend of the elbow.
- A proper distance (at least 1m) should be maintained between healthy individuals and those having coughing, sneezing, and fever. Mass gatherings and crowding at places should be avoided.
- If any person with any experience of fever, cough and breathing difficulty has traveled to any of the countries reporting COVID-19 cases or had close contact with a confirmed/suspected case of COVID-19 within 28 days should be reported immediately to the health facility.
- According to WHO, healthy person doesn't have need to use face masks. Facemasks are recommended for only those people who show symptoms of COVID-19, which help to prevent the spread of the virus to others. Health workers and people who are taking care of a suspected or a confirmed case in close settings (at home or in a health care facility) must be use the facemasks. If a mask is worn, a medical mask is to be used, ensuring that it fits well and that there are no gaps between the mask and the face. Masks should be discarded in a closed bin when it is damp, followed by hand hygiene. Touching to nose, mouth, and eyes should avoid when the mask is on.
- Environmental hygiene is also an important part of prevention it should be maintained especially in common areas used by employees like restrooms and canteens. Studies suggest that the COVID-19 virus may persist on surfaces for a few hours or up to several days and, therefore regular cleaning and disinfection of frequently touched objects and surfaces using regular disinfectants is necessary.
- Visiting to live animal markets, wet markets, or animal product markets should be prohibited. Consumption of raw or undercooked animal products should be avoided, and all the times personal hygiene should be maintained.
- Quarantine is separating a person or group of people who have been exposed to the COVID-19 case but have not yet developed illness (symptoms) from others who have not been exposed, in order to prevent the person-person spread of the virus. The duration of quarantine depends on the incubation period of COVID-19, which is 14 days from the last date of exposure [18].
- The use of particulate respirator such as certified N95 or FFP2 when performing aerosols generating procedures and to use medical masks while providing any care to suspected or confirmed cases are recommended health care workers [19].

8. Therapeutic options

In present situation, treatment of COVID-19 infection is carried out by means of repurposing existing drugs with proven safety and toxicology profiles. Among several advantages of drug repurposing, high probability of success rate, readily available information regarding their synthesis steps, manufacturing processes to foresight regarding different phases of clinical testing are few of the important ones. Moreover, repurposing existing medications to treating patient those infected by the virus in a novel way, is the best cut short path in epidemic situations. Manually reviewed information on the discovery and development of broad-spectrum antiviral agents (BSAAs) is provided by Drug Virus information database, summarizing activities and developmental statuses of 118 compounds which are safe for humans while targeting 83 human viruses. When this compounds are queried against HCoV-229E, HCoV-NL63, HCoV-OC43, MERS-CoV, SARS-CoV and novel SARS-CoV-2 then it is observed that total of fifty one compounds may be effective in prophylaxis and treatment of candidates suffering from COVID-19 infection. In this case most of these compounds demonstrated cell culture level antiviral activity including nitazoxanide, remdesivir, emetine and Memantine has been studied upto animal model level. Favipiravir is in Phase II clinical trial. Remdesivir, hydroxychloroquine and ritonavir are in advanced stage of Phase III clinical trials against novel SARS-CoV-2. In Wuhan and Shenzhen, recent clinical trial conducted on 200 patients at hospitals with an influenza medicine favipiravir, is effective against the new coronavirus. Patient within 4-11 days tested negative with no side effects, when administered with Favipiravir, in control group. Galidesivir, a nucleoside RNA polymerase inhibitor, disrupting the viral replication and shown active response against coronavirus.

Recent report proved that chloroquine and hydroxychloroquine as an effective antiviral therapeutic treatment against COVID-19 with faster recovery time. A significant elimination of virus was observed when azithromycin added to hydroxychloroquine. On the other hand, United States Centers for Disease Control and Prevention (US CDC) research shows that chloroquine is a potential prophylactic (preventative) measure against coronavirus. In China, Thailand, Japan and India, many

doctors are administering anti-HIV drugs like lopinavir and ritonavir alone and sometimes in combination with other drugs including anti-malarial chloroquine cautiously on case by case basis to treat coronavirus infected patients.

According to the guidelines of National Health Commission (NHC) of the People's Republic of China, antivirals including interferon alpha (IFN-α), lopinavir / ritonavir, and ribavirin are recommended for tentative treatment of COVID-19 with recent addition of chloroquine phosphate and arbidol after their positive preliminary clinical studies (figure 5). The duration of treatment shall not be more than 10 days. Administration of same recommendations for adults is, vapor inhalation at a dose of 5 million U (and 2 ml of sterile water for injection) 2 times per day is the recommended method of IFN-α administration. Lopinavir / Ritonavir at a dose of 400 mg/100 mg 2 times per day. Intravenous infusion at a dose of 500 mg ribavirin in combination with lopinavir / ritonavir or IFN-α 2-3 times per day. Oral administration of chloroquine phosphate 2 times per day at a dose of 500 mg. Oral administration of umifenovir (arbidol) is 3 times per day at a dose of 200 mg. The patients with high fever exceeding 38.5 °C body temperature can be cautiously administered with common drugs such as ibuprofen 5–10 mg/kg or paracetamol 10–15 mg/kg orally.

The ongoing study on HIV protease inhibitor, lopinavir along with ritonavir for the treatment of MERS and SARS coronaviruses were announced by Abbvie Inc. headquartered at North Chicago, Illinois, United States and Cipla Limited headquartered at Mumbai, India. Lopinavir is already an approved treatment against HIV infection under trade name Kaletra and Lopimune respectively. Lopinavir / Ritonavir in combination with ribavirin in an open clinical trial showed milder disease course and reduced fatality rate in patients, during 2003 SARS outbreak. Keeping in view of these positive results, several clinical trials of lopinavir are underway, either alone or in combination with other drugs such as umifenovir, oseltamivir and baloxavir marboxil. Darunavir, a protease inhibitor approved for HIV-1 treatment along with a boost agent marketed by Janssen Pharmaceutical Companies, a subsidiary of Johnson & Johnson, has donated this drug for further research as a treatment for COVID-19. A clinical trial was registered by group of researchers in China have a after the anecdotal reports, suggests its potential antiviral activity against COVID-19. Ascletis Pharma, Chinese drug maker started testing a cocktail of danoprevir and ritonavir, one approved for HIV and another approved for Hepatitis C against COVID-19. 11 patients enrolled with coronavirus-caused pneumonia are considered for ongoing Phase-I studies. A clinical trial registered by Zhengzhou Granlen PharmaTech with azvudine an experimental reverse transcriptase inhibitor drug against HIV-1/AIDS and testing in combination with marboxil/favipiravir and lopinavir/ritonavir as a potential COVID-19 treatment. For developing HIV drugs against COVID-19, it is preferable to target virus-specific proteins such as the RNA-dependent RNA polymerase keeping in view of the fact that coronaviruses does not contain or use reverse transcriptase like HIV noted painter [20].

To provide a quick response on disease, there is need to treat the emerging novel coronavirus that causes global impact throws spotlight on developing monoclonal antibody-based passive immunotherapy. Even though there is a major progress towards the development of monoclonal antibody therapy for coronavirus infection but no one monoclonal antibodies have yet been successfully marketed. The specific neutralizing monoclonal antibodies could effectively block the entry of virus either against receptor-binding domain (RBD) in spike protein or specific antibody that binds to angiotensin-converting enzyme 2 (ACE2). As the same host cell surface receptor used by both SARS-CoV and SARS-CoV-2, potential blocking agents or strategies tested to prevent SARS entry could be evaluated against SARS-CoV-2. It is reported that the RBD region of S protein of SARS-CoV targeted by a series of human monoclonal antibodies. The promising results showed by the monoclonal antibodies targeting spike protein in SARS-CoV and MERS-CoV in vitro and in vivo, that could be potentially effective against SARS-CoV-2. For effective disease prevention, the combination of different monoclonal antibodies that recognizes different epitopes on the viral surface could be assessed to neutralize wide range of isolates including escape mutants and best candidates could be used for passive immunotherapy. More potent anti-viral activity may exhibit by monoclonal antibody cocktail that could increase the effectiveness of the treatment and prevent the viral escape. In suitable expression system such as mammalian, yeast or plant the sequences of monoclonal antibodies that are effective against SARS-CoV could be cloned and recombinant monoclonal antibodies could be tested against SARS-CoV-2 [21].

The herbs when combined with modern medicine and life support system under proper observation are found to work best. The research must be carried on rapidly to investigate the chemical constituent completely effective for treating the infection. It is stated that for treating the symptoms of SARS-CoV3CL, the flavonoid extracted from the Litchi seeds can be used which inhibiting the proteinase activity (essential for viral protein synthesis). In Jinyinthan Hospital in Wuhan from where the coronavirus started, some of the patients infected with novel coronavirus (2019-nCoV) were found to be cured with traditional Chinese medicine or with combination of herbal and allopathic medicine [22]. Plant derived compounds including baicalin, scutellarin, hesperetin, glycyrrhizin and nicotianamine could interact with ACE2. Therefore, these compounds as well as herbs containing these ingredients may have the capacity to inhibit the infection of SARS-CoV-2 [23]. In India, Central Council for Research in Homeopathy also suggest the various homoeopathy perspectives in the treatment of COVID-19 infection.

A drug screening in silicon and an enzyme activity test is performed by a joint research team of the Shanghai Institute of Materia Medica and Shanghai Tech University, and they reported 30 agents with potential antiviral activity against SARS-CoV-2 on January 25, 2020 (19). These agents are indinavir, saquinavir, lopinavir, carfilzomib, ritonavir, remdesivir, atazanavir, darunavir, tipranavir, fosamprenavir, enzaplatovir, presatovir, abacavir, aortezomib, elvitegravir, maribavir, raltegravir, montelukast, deoxyrhapontin, polydatin, chalcone, disulfiram, carmofur, shikonin, ebselen, tideglusib, PX12, TDZD-8, cyclosporin A, and cinanserin. The same study also found that Chinese herbal medicines such as Rhizoma Polygoni Cuspidati and Radix Sophorae Tonkinensis may contain active ingredients against SARS-COV-2 [24].

Some important therapeutic option

Chloroquine

On SARS-CoV infection of primate cells, chloroquine has strong antiviral effects. These inhibitory effects are observed when the cells are treated with the drug either before or after exposure to the virus, suggesting both prophylactic and therapeutic advantage. The drug appears to interfere with terminal glycosylation of the cellular receptor angiotensin-converting enzyme 2 is due to elevations of endosomal pH, which is the well-known functions of chloroquine such as the drug. This may negatively influence the virus-receptor binding and abrogate the infection, with further ramifications by the elevation of vesicular pH, resulting in the inhibition of infection and spread of SARS CoV at clinically admissible concentrations [25]. At low micromolar concentration of chloroquine, it was found to block SARS-CoV-2 infection, with a half-maximal effective concentration (EC50) of 1.13 μM and a half-cytotoxic concentration (CC50) greater than 100 μM [25].

Hydroxychloroquine

In a recent trial on COVID-19 patients, 100% of patients treated with hydroxychloroquine in combination with the macrolide antibiotic i.e. azithromycin were virologically cured comparing with 57.1% in patients treated with hydroxychloroquine alone, and 12.5% in the control group. Recently, in patients with pneumonia caused by 2019-nCoV, chloroquine and hydroxychloroquine are tested and chloroquine as preventative medicine for COVID-19 [26]. In present situation, India play an important role in order to fulfill the world requirement of hydroxychloroquine.

Favipiravir

Favipiravir is a new type of RNA-dependent RNA polymerase (RdRp) inhibitor. It is capable of blocking the replication of flavi-, alpha-, filo-, bunya-, arena-, noro-, and other RNA viruses along with its anti-influenza virus activity. Favipiravir is converted into an active phosphoribosylated form (favipiravir-RTP) in cells and is recognized as a substrate by viral RNA polymerase, thus inhibiting RNA polymerase activity. Therefore, favipiravir may have potential antiviral action on SARS-CoV-2 [24].

Teicoplanin

It is especially used in Staphylococcal infections but currently, usedvin the treatment of Gram-positive bacterial infection. It has already showed efficacy against various viruses such as ebola, influenza virus, flavivirus, hepatitis C virus, HIV virus and on coronavirus such as MERS-CoV and SARS-CoV. Teicoplanin acts on the early step of the coronavirus life cycle by inhibiting the low pH cleavage of the viral spike protein by cathepsin L in the late endosomes thereby preventing the release of genomic viral RNA and the continuation of virus replication cycle [27].

Arbidol

In China and Russia arbidol is approved for influenza treatment. It had inhibitory effects on SARS, as shown by in-vitro studies [28].

Nitazoxanide

At a low-micromolar concentration it inhibited the 2019-nCoV. Nitazoxanide is a commercial antiprotozoal agent with an antiviral potential against a broad range of viruses including human and animal coronaviruses [29].

Nafamostat

A potent inhibitor of MERS-CoV, which prevents membrane fusion, was inhibitive against the 2019-nCoV infection [29].

Remdesivir

Remdesivir inhibited viral infection efficiently in a human cell line (human liver cancer Huh-7 cells), which is sensitive to 2019-nCoV. It has been recently recognized as a promising antiviral drug against a wide array of RNA viruses (including SARS/MERS-CoV5) infection in cultured cells, mice and nonhuman primate (NHP) models [29]. At low micromolar concentrations remdesivir potently blocks SARS-CoV-2 infection and has a high selectivity index (half-maximal effective concentration (EC50) is 0.77 μM; half-cytotoxic concentration (CC50) > 100 μM; SI > 129.87). It is also reported that remdesivir yielded promising results in the treatment of a patient with COVID-19 in the United States [24].

Darunavir

In China, researchers announced that darunavir inhibit SARS-CoV-2 infection in vitro. It is indicated in cell experiments that darunavir significantly inhibited viral replication at a concentration of 300 μM in vitro and that its inhibition efficiency in untreated group was 280-fold [24].

Ribavirin

Ribavirin is a broad-spectrum of antiviral effects and it is a nucleoside analogue.in study, comparision is done between 111 patients with severe acute respiratory syndrome (SARS) treated with ribavirin monotherapy and 41 patients with SARS treated with lopinavir/ ritonavir and ribavirin. There is low risk of acute respiratory distress syndrome (ARDS) and death when patients treated with the combined therapy [24].

Oseltamivir

In a study, a total of 35 patients received oseltamivir (37.6%) on possible MERS-CoV cases in Paris from 2013 to 2016. Oseltamivir was given to patients with positive for influenza virus (n = 25), 52% (n = 13) and it was concluded that empirical oseltamivir can be started in suspected MERS-CoV cases. Many other studies also evaluated oseltamivir in MERS-CoV. In the management of 2019-nCoV oseltamivir is used. However, definite evidence of efficacy is inconclusive because of lack of suitable control group in the studies [30].

Lopinavir/ritonavir

In the treatment of HIV, ritonavir boosting along with lopinavir is used. A clinical study at the same Hong Kong University suggests that even after adjustment for LDH level (possible confounder), a significant association was seen between lopinavir/ritonavir use and better outcome. As per the current guidelines, for the treatment of 2019-nCoV, lopinavir and ritonavir is the recommended protease inhibitor [30].

Interferon

Interferons (IFNs) are broad-spectrum antivirals, primarily used in the treatment of hepatitis B. In compared to ribavirin

or IFN alone, observed that IFN-α along with high-dose corticosteroid group is beneficial in SARS-CoV patients. Other observational studies also support these findings and combined use of IFN-α and corticosteroid showed less disease-associated oxygen saturation impairment. IFN-α (5 million U bid inh) is advised along with lopinavir and ritonavir combination for the treatment of 2019-nCoV [30].

Immunoglobulins

In the critically case of SARS, who show signs of deterioration, further escalation of immunomodulation is indicated and intravenous (i.v.) immunoglobulin may be considered. Patients may get benefit from i.v. immunoglobulin who show poor response to initial empirical therapy [30].

Corticosteroids

For the treatment of SERS-CoV and MERS-CoV corticosteroids were widely used and are also used in the management of the current epidemic of 2019-nCoV. However, the use of routine corticosteroids prohibited unless indicated for other clinical ground by the interim guidelines of WHO. Use of corticosteroid is reported to be associated with delayed clearance of viral RNA (both in case of SERS-CoV and MERS-CoV) and other steroid-related complications such as psychosis [30].

For severe ARDS the use of corticosteroids is controversial; therefore, the use of glucocorticoids systemically is prohibited. Methylprednisolone can be used as appropriate for patients with rapid disease progression or severe illness. According to the severity of the disease, 40 to 80 mg of methylprednisolone per day can be considered, and the total daily dose should not exceed 2 mg/kg [31].

Antibiotics

According to the clinical manifestations of patients, if the accompanying bacterial infection cannot be ruled out, mild patients can take antibacterial drugs against community-acquired pneumonia, such as amoxicillin, azithromycin, or fluoroquinolones; empirical antibacterial treatment in severe patients should cover all possible pathogens, deescalating therapy until the pathogenic bacteria are clarified [31].

Oxygen therapy

In this, nasal catheter, mask oxygen, high flow nasal oxygen therapy (HFNO), non-invasive ventilation (NIV) or invasive mechanical ventilation are included. First, for patients with severe respiratory infections, respiratory distress, hypoxemia or shock, Oxygen therapy is the choice. The initial flow rate is 5 L/min, and the titration flow rate is to reach the target oxygen saturation (adults: $SpO_2 \geq 90\%$ in non-pregnant patients, $SpO_2 \geq 92–95\%$ in pregnant patients; children: $SpO_2 \geq 94\%$ in children with obstructive dyspnea, apnea, severe respiratory distress, central cyanosis, shock, coma or convulsions, and $\geq 90\%$ in other children).

Later, patients with hypoxic respiratory failure and acute respiratory distress syndrome should be given respiratory support to. HFNO or NIV can be selected when nasal cannula or mask oxygen therapy was ineffective or the patient had hypoxic respiratory failure. However, HFNO oxygen is not the routinely adopted when patients had hypercapnia (acute exacerbation of chronic obstructive pulmonary disease, cardiogenic pulmonary edema), hemodynamic instability, multiple organ failure, and abnormal mental status. Intubation should be performed immediately if respiratory failure cannot be improved or worsens continuously within a short time (1 h) after using HFNO or NIV. Low tidal volume (4-8 ml/kg) and low suction pressure (platform pressure $< 30 cmH_2O$) are used for invasive mechanical ventilation. It is suggested that positive end-expiratory pressure (PEEP) with high positive end-expiratory pressure should be used in patients with moderate or severe acute respiratory distress syndrome, and PEEP should be titrated according to FiO_2 to maintain SpO_2, in order to improve alveolar atelectasis and reduce alveolar hyper-expansion and pulmonary vascular resistance at the end of inspiration. Ventilation is recommended in prone position for severe patients with acute respiratory distress syndrome (ARDS) for more than 12 h/d. the patients with refractory hypoxemia that is difficult to be corrected by protective lung ventilation should be recommended Extracorporeal Membrane Oxygenation (ECMO) [31].

9. Conclusion

A novel coronavirus produce a serious respiratory infection i.e. COVID-19. Presently, it produces a threat to global issue to control its spread and to reduce the mortality as soon as possible. Presently, different health professional in world continuously tried to control the progress of disease in patient and at certain level they get succeed. On other hand, the different world scientist continuously work on discovery of effective drug therapy and development of vaccine against COVID-19. The present review focus on structure of corona virus, etiology, pathogenesis, diagnosis, clinical features, prevention and current therapy. The ultimate aim of present review article is to aware the community about SARS coronavirus and its infection as well as this review study try to provide a data for curious scientific professionals who can contribute their efforts to fight such threatening infections.

10. References

1. Zhong NS, Zheng BJ, Li YM, Poon LLM, 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. 2003; 362(9393):1353-1358.
2. Cheng VCC, Lau SKP, Woo PCY, Yuen KY. Severe Acute Respiratory Syndrome Coronavirus as an Agent of Emerging and Reemerging Infection. Clinical Microbiology Reviews. 2007; 20(4):660–694.
3. Loeffelholz MJ, Tang Y. Laboratory diagnosis of emerging human coronavirus infections – the state of the art. Emerging Microbes & Infections. 2020; 9(1):747-756.
4. Cui J, Li F, Shi Z. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol. 2019; 17:181–192.
5. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research. 2020; 24:91-98.
6. Fehr AR, Perlman S. Coronaviruses: An Overview of Their Replication and Pathogenesis. In: Maier H., Bickerton E., Britton P. (eds) Coronaviruses, Methods in Molecular Biology. Humana Press, New York. 2015; 1282:1-23.
7. Chan JF, To KK, Tse H, Jin DY, Yuen KY. Interspecies transmission and emergence of novel

viruses: lessons from bats and birds. Trends Microbiol. 2013; 21(10):544-55.
8. Chen Y, Liu Q, Guo D. Emerging coronaviruses: Genome structure, replication, and pathogenesis. J. Med. Virol. 2020; 92(4):418-423.
9. Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, *et al*. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. Emerg Microbes Infect. 2020; 9(1):221-236.
10. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, *et al*. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N. Engl. J. Med. 2020; 382(13):1199-1207.
11. Bauch CT, Lloyd-Smith JO, Coffee MP, Galvani AP. Dynamically modeling SARS and other newly emerging respiratory illnesses: past, present, and future. Epidemiology. 2005; 16(6):791-801.
12. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, *et al*. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology. 2020; 295(1):202-207.
13. 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. 2020; 395:497-506.
14. Weiss SR, Navas-Martin S. Coronavirus Pathogenesis and the Emerging Pathogen Severe Acute Respiratory Syndrome Coronavirus. Microbiology and Molecular Biology Reviews. 2005; 69(4):635–664.
15. Hassan S, Sheikh FN, Jamal S, Ezeh J, Akhtar A. Coronavirus (COVID-19): A Review of Clinical Features, Diagnosis, and Treatment. Cureus. 2020; 12(3):e7355.
16. Yi Y, Lagniton PNP, Ye S, Li E, Xu RH. COVID-19: what has been learned and to be learned about the novel coronavirus disease. Int J Biol Sci. 2020; 16(10):1753-1766.
17. Rahman S, Bahar T. COVID-19: The New Threat, Int J Infect. 2020; 7(1):e102184.
18. Ramesh N, Siddaiah A, Joseph B. Tackling corona virus disease 2019 (COVID 19) in workplaces, Indian J Occup Environ Med. 2020; 24(1):16-8.
19. Adhikari PS, Meng S, Wu Y, Mao Y, Ye R, Wang Q, *et al*. A Literature Review of 2019 Novel Coronavirus during the Early Outbreak Period: Epidemiology, Causes, Clinical Manifestation and Diagnosis, Prevention and Control. Preprints, 2020, 2020020060.
20. Basha SH. Corona virus drugs–a brief overview of past, present and future. J Peer Scientist. 2020; 2(2):e1000013.
21. Shanmugaraj B, Siriwattananon K, Wangkanont K, Phoolcharoen W. Perspectives on monoclonal antibody therapy as potential therapeutic intervention for Coronavirus disease-19 (COVID-19). Asian Pacific J Allergy and Immunology. 2020; 38(1):10-18.
22. Dudani T, Saraogi A. Use of Herbal Medicines on Coronavirus, Acta Scientific Pharmaceutical Sciences. 2020; 4(4):61-63.
23. Yang Y, Islam MS, Wang J, Li Y, Chen X. Traditional Chinese Medicine in the Treatment of Patients Infected with 2019-New Coronavirus (SARS-CoV-2): A Review and Perspective. Int J Biol Sci. 2020; 16(10):1708-1717.
24. Dong L, Hu S, Gao J. Discovering drugs to treat coronavirus disease 2019 (COVID-19). Drug Discoveries and Therapeutics. 2020; 14(1):58-60.
25. Vincent MJ, Bergeron E, Benjannet S, *et al*. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J. 2005; 2:69.
26. Rosa SGV, Santos WC. Clinical trials on drug repositioning for COVID-19 treatment. Rev Panam Salud Publica. 2020; 44:e40.
27. Baron SA, Devaux C, Colson P, Raoult D, Rolain JM. Teicoplanin: an alternative drug for the treatment of coronavirus COVID-19. Int. J. Antimicrob Agents, Article 2020, 105944.
28. Zhang J, Zhou L, Yang Y, Peng W, Wang W, Chen X. Therapeutic and triage strategies for 2019 novel coronavirus disease in fever clinics. The Lancet Respiratory Medicine. 2020; 8(3):e11-e12.
29. Wang M, Cao R, Zhang L, *et al*. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res. 2020; 30:269–271.
30. Sarma P, Prajapat M, Avti P, Kaur H, Kumar S, Medhi B. Therapeutic options for the treatment of 2019-novel coronavirus: An evidence-based approach. Indian J. Pharmacol. 2020; 52(1):1-5.
31. Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, *et al*. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res. 2020; 7:4.