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REVIEW ARTICLE

The Emergent Pandemic- A Review on Coronavirus SARS-Cov-2: Virology, Pathogenesis and Outbreak

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Abstract

The coronaviruses have been found to affect the human life and ecosystem since past few years now. First the SARS (severe acute respiratory syndrome), then MERS (Middle East respiratory syndrome) and now the recent infection caused by yet another category of coronaviruses have proved to be fatal to human life. In December 2019, few cases of pneumonia of unknown cause were reported in the Hubei province of Wuhan City, China. Later after thorough investigations it was found that these patients were infected with a new viral infection caused by yet another type of coronavirus and called it severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Previously it was named as novel coronavirus disease 2019 (2019-nCoV). This infection within a small duration of time affected a huge population in more than 200 regions/countries with numerous deaths. It has now emerged as a pandemic disease with severe complications to mankind. Considering the threat of this infection, it is need of the hour to have a thorough knowledge of coronaviruses. The changing pattern of disease spread in various regions has made it necessary to carry out further research in this filed. Also considering the risk factors associated with COVID-19 infection, it is important to learn and research the virology of this infection in detail. In this review the general characteristics, origin, structure, genomics, pathogenesis, transmission, clinical features, lab investigations, radiological features, and overall features associated with coronaviruses and COVID-19 especially with prevention of this hazardous disease are discussed with an aim to generate awareness and control the spread of this global health crisis.

Keywords

Coronaviruses, SARS, MERS, COVID-19, Virology, Pathogenesis

Abbreviations

CoVs: Coronaviruses; WHO: World Health Organization; SARS: Severe Acute Respiratory Syndrome; MERS: Middle East Respiratory Syndrome; COVID-19: Coronavirus disease-19

Introduction

The global ecosystem has been in a constant state of alteration especially so in the recent years. The consistent environmental variations and the change in the living culture have led to an increased interaction of the animal life with the human life. Some of the chief microorganisms responsible for causing infections in humans fall under the category of coronaviruses. These groups of viruses tend to colonize and infect the respiratory, gastrointestinal, hepatic and central nervous systems of not just human beings but also seem to be present in birds, bat, mouse, and many other wild animals [1]. After the detection of new pneumonia cases in December 2019 in China, a number of investigations were carried out by various laboratories. The reason behind these investigations was the unknown cause of so many sudden pneumonia cases among the population. Later it was found that these patients were positive for a new viral infection caused by yet another type of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was named as novel coronavirus disease 2019 (2019-nCoV) on 12 January 2020 by the World Health Organization. Later the WHO named this infection as

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the coronavirus disease-19 (COVID-19) on 11 February 2020 [2]. On 11th March, 2020 the WHO declared it as a pandemic disease.

The new COIVD-19 infection has said to be affected 5,165,481 cases with 336,430 deaths and has spread to about 216 countries up to 24th May, 2020 5.30 pm GST (https://www.who.int/emergencies/diseases/novel-coronavirus-2019?gclid=EAIaIQobChMIlsmk4Lb-M6QIVClRgCh0A1QttEAAYASAAEgIxZvD_BwE). The COVID-19 infection has proved to be spreading at a quick pace all over the world and has caused a dangerous amount of human loss. The main reason to this loss is the human to human spread of COVID-19 infection. Also it has been reported that most of the infected person show asymptomatic stages called as silent carriers. Hence the aim globally should focus to stop and control its human to human spread as much as possible by following the possible precautions [3].

Due to dynamic deviations of the climate and ecology, the communications of human with animals has enhanced. With this comes an increased risk of emergence of many such infectious diseases in the near future. Hence, there is a dire need to study the origin, virology, transmission, prevention and necessary precautions related to these emerging health crises. It is also likely to investigate and research the possible immune responses and vaccines against these viral infections. For conducting research, the absolute knowledge about the course and pattern of the disease spread also becomes essential.

Origin, History and Taxonomy

The coronaviruses have been thought to be emerged and are prevalent since decades now in the ecosystem. Their origin is mainly thought to be in different mammals and is reported to infect the vertebrates. Since the 19th century the study of coronaviruses has been a topic of research. Studies state that the coronaviruses belong to the subfamily of Orthocoronavirinae of the Coronaviridae family of the order Nidovirales [4]. They are further classified into four another genera of CoVs namely-

Alphacoronavirus (alphaCoV),

Betacoronavirus (betaCoV),

Deltacoronavirus (deltaCoV), and

Gammacoronavirus (gammaCoV) [1].

The betaCoV genus is further classified into five sub-genera or lineages. Genomic representation has shown that possibly bats and rodents are the gene sources of alphaCoVs and betaCoVs. On the other hand certain bird species tend to denote the gene sources of deltaCoVs and gammaCoVs. It can't be denied that the coronaviruses are a huge group of viruses reported to cause infections in different animal species, comprising of camels, cattle, cats, and bats. Out of these varied viruses seven among the group have reported to cause infections in human and hence are titled as Human CoVs (HCoVs). Some of these were found in 1960's but most of them are found in the recent years [4].

As reported in one of the studies the Coronaviridae is a monogeneric family comprising 11 viruses which infect vertebrates. The group was formerly documented on the basis of typical virion morphology (Tyrrell, et al. 1968), but can now be well-defined by biological and molecular principles [5].

Before the outbreak of COVID-19, the other two infections from coronavirus that emerged as health emergencies were the SARS-CoV and MERS-CoV outbreaks [2]. These two strains of coronavirus have hopped species from animal to humans, and further spread by person-to- person transmission, and caused severe acute respiratory syndrome leading to high death rate in the past 2 decades [6]. Severe acute respiratory syndrome-associated virus (SARS-CoV), previously unknown coronavirus traced to horseshoe bats in southern China, caused 8,096 positive cases and 774 deaths (9.6% fatality rate) in 29 countries from November 2002 to July 2003 [7]. In 2012, another viral disease called Middle East respiratory syndrome (MERS) emerged in the Middle East. It was reported to be caused by a virus originally named as the human coronavirus-Erasmus Medical Center/2012 (HCoV-EMC/2012), but was later renamed as Middle East respiratory syndrome coronavirus (MERS-CoV) [8]. MERSCoV is comparable to severe acute respiratory syndrome coronavirus (SARS-CoV), which killed almost 10% of the affected individuals in China between 2002 and 2003 [4]. The first MERS patient reported in Saudi Arabia in June 2012 was possibly infected by direct or indirect transmission of the virus from dromedary camels [6,8].

The initial outbreak of COVID-19 was reported as few pneumonia cases of unknown etiology which was later confirmed by CDC (center for disease control) China that it's a novel coronavirus. It was first detected to be transmitted from bats to humans and later spread by human to human transmission [3].

Chan, et al. reported that the genome of the new HCoV, isolated from a group of patients with atypical pneumonia from Wuhan, had 89% nucleotide identity with bat SARS-like-CoVZXC21 and 82% with that of human SARS-CoV. Therefore, the new virus was called SARS-CoV-2. Even though its origins are not completely agreed, these genomic studies propose that SARS-CoV-2 possibly developed from a strain found in bats or bat droppings. This was probably originated at the huge seafood market in the city of Wuhan as per reports. The probable augmenting mammalian host which is supposed to be a medium between bats and humans, is, conversely, not known yet [4].

Structure, Genomics and Virology

Coronaviruses are enveloped, non-segmented, pos-

itive-sense single-stranded RNA virus genomes in the size ranging from 26 to 32 kilobases [9]. Coronavirions are pleomorphic, even though commonly spherical, 60 to 220 nm in diameter and bear widely spaced, club-shaped surface projections about 20 nm in length. Complete virions have a density in sucrose of about 1.18 g/ml. In thin sections the virion envelope may be pictured as inner and outer shells separated by a translucent space [5]. They are one of the largest known viral RNA genome. The virion has a nucleocapsid composed of genomic RNA and phosphorylated nucleocapsid (N) protein, which is covered within phospholipid bilayers and covered by two different types of spike proteins: The spike glycoprotein trimmer (S) that can be found in all CoVs, and the hemagglutinin-esterase (HE) that exists in some CoVs. The membrane (M) protein (a type III transmembrane glycoprotein) and the envelope (E) protein are situated among the S proteins in the virus envelope. Coronaviruses were specified their name based on the characteristic crown-like appearance [9].

The coronavirus genome is a linear molecule of single-stranded RNA which is polyadenylated and infectious. The genome RNA has a molecular weight of 5×10^6 to 7×10^6, corresponding to about 15000 to 20000 nucleotides. T_1-resistant oligonucleotide fingerprinting of genome RNA and intracellular viral mRNA confirms the positive polarity of the genome and indicates that it does not have extensive sequence reiteration [5].

In addition to RNA the coronavirion nucleocapsid contains a non-glycosylated protein of 50000 to 60000 mol. wt. This protein is phosphorylated and purified murine hepatitis virus (MHV) virions have been shown to contain a protein kinase activity. Coronavirions contain two major envelope proteins [6]. The matrix protein is a transmembrane glycoprotein of 20000 to 35000 mol. wt., the carbohydrate moiety of which is known for MHV and bovine coronavirus (BCV) to be O-glycosidically linked. The glycosylated region of the protein is exterior to the virion envelope and in many cases matrix proteins with different degrees of glycosylation are incorporated into virions. Glycosylation is most likely to be at the N-terminus of the polypeptide. The second coronavirion envelope protein, which constitutes the surface peplomer, is responsible for eliciting neutralizing antibodies during infection [5].

Two or 3 structural proteins are associated with viral envelop. The matrix protein (M) embedded in envelop. The spike structural protein (S) anchored in envelop is target of neutralizing antibody. The coronaviruses have 5 essential genes which are for 4 structural proteins (N, E, M, S) and for viral replication/transcription (RNA dependent RNA polymerase, RdRp). The genome organization is 5'-RdRp-S-E-M-N-3'. This gene order of coronaviruses is highly conserved [6]. The study of virus lipid envelope has been studied in detail since decades now. The virion envelope contains phospholipids, glycolipids, cholesterol, di- and triglycerides and free fatty acids in proportions approximately corresponding to those in the cell membrane. Cholesteryl and fatty acid esters present in cell membranes are selectively depleted in the virion membrane [5].

Pathogenesis

A number of studies suggest that SARS-CoV-2 enters a host cell by binding its spike proteins, which defines host tropism, to host cell receptors. Initial researches reported that SARS-CoV-2 might share a host cell receptor with SARS-CoV, because the 2 strains have similar receptor-binding protein structures. Consecutive studies showed that SARS-CoV-2 binds to angiotensin converting enzyme 2 (ACE2) as SARS-CoV does [6]. The host innate immune system detects viral infections by using pattern recognition receptors (PRRs) to recognize pathogen-associated molecular patterns (PAMPs). At present, the known PRRs mainly include toll-like receptor (TLR), RIG-I-like receptor (RLR), NOD-like receptor (NLR), C-type lectin-like receptors (CLmin), and free-molecule receptors in the cytoplasm, such as cGAS, IFI16, STING, DAI, and so on [9]. Since the intermediate host of SARS-CoV-2 is still not known, a number of studies are being carried out to investigate the possible interactions of the pathogen with various receptors. One such study done by Liu, et al. predicted the interaction between the receptor-binding domain (RBD) of coronavirus spike protein and the host receptor, angiotensin-converting enzyme 2 (ACE2). The interaction between the key amino acids of S protein RBD and ACE2 indicated that, other than pangolins and snakes, as previously studied and reported, turtles (Chrysemys picta bellii, Chelonia mydas, and Pelodiscus sinensis) may act as the possible intermediary hosts transferring SARS-CoV-2 to humans [10].

In CoVs, the genomic structure is organized in a +ssRNA of approximately 30 kb in length - the largest known RNA viruses - and with a 5'-cap structure and 3'-poly-A tail. Starting from the viral RNA, the synthesis of polyprotein 1a/1ab (pp1a/pp1ab) in the host is recognized. The transcription works through the replication-transcription complex (RCT) organized in double-membrane vesicles and via the synthesis of subgenomic RNAs (sgRNAs) sequences [4]. As reported, transcription termination occurs at transcription regulatory sequences, located between the so-called open reading frames (ORFs) that work as templates for the production of subgenomic mRNAs. In the atypical CoV genome, at least six ORFs can be present [2]. Among these, a frame-shift between ORF1a and ORF1b guides the production of both pp1a and pp1ab polypeptides that are processed by virally encoded chymotrypsin-like protease (3CLpro) or main protease (Mpro), as well as one or two papain-like proteases for producing 16 non-structural proteins (nsps). Apart from ORF1a and ORF1b, other ORFs encode for structural proteins, including spike, membrane, envelope, and nucleocapsid proteins and accessory proteic chains [5].

Pathophysiology and virulence activities of CoVs, and hence also of SARS-CoV-2 have links to the function of the nsps and structural proteins. For instance, research underlined that nsp is able to block the host innate immune response [4]. Among functions of structural proteins, the envelope has a crucial role in virus pathogenicity as it promotes viral assembly and release [5]. Certain studies have shown that 2019-nCoV grows better in primary human airway epithelial cells than in standard tissue-culture cells, unlike SARS-CoV or MERS-CoV [11]. Identification of the virus will let the development of reagents to report about the crucial nonentities about this new coronavirus infection and lead to the development of antiviral therapies. Understanding the sequence of the genome will facilitate the development of sensitive quantitative reverse-transcriptase-polymerase chain-reaction assays to rapidly detect the virus [10]. The development of serologic assays will permit evaluation of the prevalence of the infection in humans and in potential zoonotic sources of the virus in wet markets and other settings [11]. Another study suggests that RNA-RNA recombination in coronavirus is random and common in nature [12].

According to a new research, a spike mutation, which probably occurred in late November 2019, might have triggered infection hopping to humans [4]. Angeletti, et al. compared the SARS-Cov-2 gene sequence with that of Sars-CoV. They analyzed the transmembrane helical segments in the ORF1ab encoded 2 (nsp2) and nsp3 and found that position 723 presents a serine instead of a glycine residue, while the position 1010 is occupied by proline instead of isoleucine [13]. More research in this particular field is required to investigation the viral characteristics and pathogenic mechanisms of COVID-19.

The mechanism behind pathogenic production of pneumonia is still complicated. The overall data till date is suggestive that the viral infection can elucidate an immune reaction in the host [9]. In few examples, 'cytokine storm' labeled reaction occurs. The effect is extensive tissue damage. The protagonist of this storm is interleukin 6 (IL-6). IL-6 is produced by activated leukocytes. It is promotes the differentiation of B lymphocytes and inhibits the growth of others. It also stimulates the production of acute phase proteins and plays an important role in thermoregulation, in bone maintenance and in the functionality of the central nervous system. Although the main role played by IL-6 is pro-inflammatory, it can also have anti-inflammatory effects. It is also implicated into the pathogenesis of the cytokine release syndrome (CRS) that is an acute systemic inflammatory syndrome characterized by fever and multiple organ dysfunction [4].

Transmission

The origin, evolution, spread and overall changing patterns of transmission of these viral infections are some of the most important factors to be considered. A thorough research of transmission patterns will aid in control of spread of these viral infections around the globe. The first cases of the CoVID-19 disease were connected to direct exposure to the Seafood Wholesale Market of Wuhan city which was indicative of the animal-to-human transmission. However, later cases were not associated with the same mechanism. Therefore, it was established that the virus could also be transmitted from human-to-human transmission [4]. The coronaviruses are reported to be habitat of various mammals. Over the years, it is observed that they have potential to spread from animals to humans due to alterations in the ecosystem [1]. Even though their intermediate host is unknown, yet the origin from particular animal species is established in research studies. SARS-CoV-2 was first isolated from a bronchoalveolar lavage and RNA of the virus was also detected in nasopharyngeal and throat swabs as well as blood, stool, urine, and saliva [6]. In many cases they replicate in the respiratory tract and transmission of the virus is usually from this site, although virus is also shed with the faeces. Human and avian viruses are transmissible to mice by the intracerebral route [5]. Yet the confirmation of this information needs to be validated with the upcoming research. The binding of a receptor expressed by host cells is the first step of viral infection followed by fusion with the cell membrane. It is observed that the lung epithelial cells are the primary target of the virus. Thus, it has been reported that human-to-human transmissions of SARS-CoV occurs by the binding between the receptor-binding domain of virus spikes and the cellular receptor which has been identified as angiotensin-converting enzyme 2 (ACE2) receptor [3]. Importantly, the sequence of the receptor-binding domain of COVID-19 spikes is similar to that of SARS-CoV. This data evidently indicates that entry into the host cells is most likely via the ACE2 receptor [3,11].

Many studies have reported that the main medium of transmission of COVID-19 is by human-to-human mainly via respiratory droplet spread or either by direct contact to the patients [3]. Droplets from sneezes, cough, breathing aspirates, contacts and feces, and aerosols transmission are some of the important medium for spread of infection. This was given in accordance to the sixth version of the guidance for diagnosis and treatments for COVID-19 issued by the National Health Commission of China. Few of the studies have also mentioned about the possibility of vertical transmission from mothers to babies but still studies are being carried out on these measures and no evidences are available till date. It is still important to perform precautionary measures to protect the new born from the health outbreak [4]. A local immune response resulting in secretion of IgA is usually adequate to overcome the acute phase of disease. Coronaviruses along with acute infection readily create persistent infection in animals, often leading to diseases of a sub-acute or chronic nature [5].

Aerosol transmission has also been reported so far with COVID-19 especially in closed spaces like hospitals. Hospital acquired infection has been seen majorly in almost all the countries where the virus has spread. In the city of Wuhan, it was reported that the high number of the health care workers were infected as a result of which the health facilities could not be delivered well to all the patients. And hence there was high fatality rate in the initial months of viral spread [4].

Clinical Symptoms

As known earlier that coronaviruses mainly affect the lung parenchyma or the respiratory tissue, infections mainly show respiratory disease symptoms. According to WHO, a COVID-19 patient will show mild respiratory disease symptoms like dry cough, cold, fever and also malaise. The incubation period of COVID-19 disease is said to be reported by few studies as 5.2 days approximately. After this incubation period the patient is known to show certain signs or symptoms. The duration from the beginning of this infection symptom to death varied from 6 to 41. This range was observed to be less in individuals above the age of 70 years as compared to those below the age of 70 years. Dry cough, fever and fatigue followed by breathlessness are some of the most common symptoms of this infection. Formation of sputum, hemoptysis, headache, lymphopenia and diarrhea are few of the other symptoms associated with Covid-19 infection which are said to develop in the later course of disease [14]. Few of the respiratory disorder warning signs like dry cough, fever and dyspnea seen in Covid-19 infection are considered to be common indicators of the disease. These symptoms are found to be alike to the other two epidemic disease of SARS in 2003 and MERS in 2012 that strongly indicates droplet spread of infection and transmission by direct contact [2]. On the other hand, nausea, diarrhea, vomiting, and abdominal distress that occur not more commonly are said to have a varied population difference, with an early and mild onset often followed by classic respiratory disease indications. The potential risk factors of older age, high SOFA score, and d-dimer greater than 1 μg/mL could help clinicians to identify patients with poor prognosis at an early stage. Prolonged viral shedding provides the rationale for a strategy of isolation of infected patients and optimal antiviral interventions in the future [14].

The sequence of clinical symptoms in descending order from most common to least common are as follows as per a study- fever, cough, breathlessness or dyspnoea, myalgia, headache and diarrhoea. Rhinorrhea, sore throat and pharyngalgia according to few studies was reported in 4.0%, 5.1% and 17.4% of cases respectively [2]. It is reported that in initial stages patient might not require respiratory support. But in later stages of infection patient may require ventilation and intensive care units (ICU) [4]. It was observed that ICU required patients mainly experience breathlessness. Cardiovascular disease, hypertension and diabetes mellitus were found to be the most common underlying or secondary debilitating diseases among adult age group cases [14]. Further complications were also encountered in few patients of metabolic acidosis, shock, ARDS, coagulation dysfunction and finally multiple system organ function failure. In unfavorably diseased cases dyspnea, anorexia and abdominal pain were also present. Sepsis was also countered in most critical cases. The display of fever symptoms varied from mild to moderate in infected individuals [4].

High intake of drugs like antibiotics, anti-viral drugs, etc. can cause drug toxicity that will further cause liver injury, also could be an over response of immune system as per few reported studies. Though the exact effect of Covid-19 on liver is still to be investigated and further studies needs to be carried out. Expression of ACE2 was seen in the hepatocytes suggestive of mild liver injury to the bile ducts and associated symptoms were present. In addition, 2019-nCoV sequence could be also detected in the self-collected saliva of most infected patients even not in nasopharyngeal aspirate, and serial saliva specimens monitoring showed declines of salivary viral load after hospitalization. Although this doesn't completely mean that viral infection is present. Hence positive viral culture suggests the possibility of salivary gland infection and possible transmission. Considering few other studies too, a growing number of clinical evidence reminds us that digestive system other than respiratory system may serve as yet another route of infection when people are in contact with infected wild animals or positive patients [15].

As per one study it was reported that viral shedding was up to a minimum of 8 days to 20 days and maximum of 37 days [14].

Laboratory Investigations and Histopathology

For performing the necessary investigatory measures it is important for sample collection. Most commonly the bronchoalveolar-lavage fluid is collected from lower respiratory tract [16]. Throat swabs as well as nasal swabs can be collected. RT-PCR, sequencing of genomes and certain serological techniques like Enzyme-linked immunosorbent assay, commonly called as ELISA have been routinely used for laboratory investigations of Covid-19 infection. This is along with adjuvant radiological assessment and clinical findings. Transmission electron microscopy is as well used for examination after viral isolation [16]. Alterations in the levels of aminotransferases, plasma proteins, and prothrombin time are some of the indications of liver injury. These were seen in few of the studies. Atypical features of liver damage could be investigated by percutaneous biopsies of liver [15].

A study was carried out by Tian, et al. who studied the possible histopathological features involved in

COVID-19 infection. In this study, histopathological data was obtained on the lungs of two patients who underwent lung lobectomies for adenocarcinoma and retrospectively found to have had the COVID-19 viral infection at the time of surgery. Other than the presence of tumors, the lungs of both these cases displayed edema and important proteinaceous exudates as large protein globules. It was also reported that vascular congestion combined with inflammatory clusters of fibrinoid material and multinucleated giant cells and hyperplasia of pneumocytes were present in these patients [17].

Radiological Findings

Computed Tomography (CT) is the most commonly used diagnostic radiographic aid in COVID-19 patients. It is also considered as an accurate radiological technique in cases of Covid-19 to examine, read and study the chest findings. The most common chest radiographic findings are consolidations, opacities involving one or all the lobes of both the lungs. Most commonly seen cases had bilateral involvement. In a study chest findings were described as presence of bilateral fluffy opacities with increased density, profusion, and confluence. These changes were most commonly seen in the lower lung fields or lower respiratory compartments. Changes like presence of accumulation of pleural liquid were also visible [16]. Another study mentioned findings of linear opacities as, “crazy-paving” pattern and the “reverse halo” sign. Bernheim, et al. conducted a study to examine radiographic features seen in infected patients. It was found that bilateral lung involvement was seen in majority of the cases [18].

Treatment Outcomes

Keeping into consideration the nature and overall features of this viral infection, treatment strategies must be implemented. At present there is no vaccination or a specific medication available for COVID-19. A number of studies are undergoing in their initial stages for the invention of vaccination against COVID-19. Hence, the only measure available globally is to provide symptomatic treatment to the positive cases. As a result the first line of medications administered is the anti-viral drugs. Lopinavir and ritonavir are some of the anti-viral drugs used recently. A study conducted with the use of lopinavir and ritonavir suggested that they can be efficiently used for treating patients with COVID-19 [19]. Other drugs include the nucleoside analogues. It has to be understood that till any particular medicine is standardized other drugs must be used. Drugs that have the potential to diminish the virus infection like HIV-protease inhibitors are being used [2]. Ganciclovir, oseltamivir and lopinavir or ritonavir tablets are few of the anti-viral drugs prescribed as per current study reports. It was also reported that 90% of the positive patients are administered with few broad spectrum antibiotics [3].

It has to be taken into account that there is no standardized treatment for COVID-19. Lopinavir/ritonavir, neuraminidase inhibitors, nucleoside analogues, remdesivir, umifenovir, tenofovir, disoproxil and lamivudine which are DNA synthase inhibitors, chloroquine, traditional medicines from China, etc. are some of the group of drugs that have been used in this global health crisis [2]. The pharmacological properties of Chloroquine have been described by certain studies to be associated with inhibition of few viral proteins resulting into inhibition of important pathways in viral replication/activation. Hydroxychloroquine has been widely used in many countries and proved to be effective. Few studies are being carried out to test the effectiveness of azithromycin in treating COVID-19. One such study carried out by Gautret, et al. suggested that hydroxychloroquine is strongly related to diminishing the viral activity or load and its effect is enhanced in presence or in adjuvant to azithromycin drug [20]. A number of studies are under progress to test the efficacy of azithromycin in controlling Covid-19. Also, use of convalescent plasma in treatment of this pandemic is under trials. Few studies have been carried out on the use of plasma transfusion in treating Covid-19 patients but there are certain limitations with the same [21]. As a result of which more research studies must be carried out for further inventions. Many of the countries have encouraged research in this field.

Prevention and Precautions

Accepting the current scenario and facts about absence of any vaccine and specific treatment to this disease, infection prevention measures are of utmost importance. The preventive strategies mainly should focus on limiting the spread of disease which can be reduced by avoiding contact with infected person and also by maintaining self-hygiene. Special importance must be given to critical procedures like collection of samples from patients and proper training must be administered. Strict protocols must be followed in hospitals and wards to reduce hospital acquired infections especially to the health workers. The high risk group individuals like the old age groups, patients with secondary debilitating diseases and new born must be taken care with appropriate measures [3]. A number of protocols and measures have been stated by the WHO. Few of the protocols to be strictly followed mentioned by WHO are as follows-

- Avoid close contact with subjects suffering from acute respiratory infections.
- Wash your hands frequently, especially after contact with infected people or their environment.
- Avoid unprotected contact with farm or wild animals.
- People with symptoms of acute airway infection should keep their distance, cover coughs sneezes with disposable tissues or clothes and wash their hands.

- Strengthen, in particular, in emergency medicine departments, the application of strict hygiene measures for the prevention and control of infections.
- Individuals that are immunocompromised and also others should avoid public gatherings.

Also, for early prevention of disease spread travel history is the most important factor to be taken into consideration [4]. Regular washing of hands, sanitizing it from time to time after contact with infected surroundings, avoiding direct contact with positive patients, use of optimal protective measures like covering mouth with any cloth or mask and practicing personal cleanliness are few of the other measures to be followed. People with any kind of signs and symptoms associated with COVID-19 should immediately get themselves examined and tested as early as possible. Infection prevention and control practices that are standardized are prescribed to be followed by health care units and hospitals [2]. Certain protocols and guidelines have also been formulated by The US Centers for Disease Control and Prevention (CDC) that mentioned a detailed history of people coming from other parts of the world to be taken into account. Like all other CoVs, COVID-19 is also sensitive to ultraviolet rays and heat. Moreover, these viruses can be effectively inactivated by lipid solvents including ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform except for chlorhexidine [4]. Hence, hand and material sanitizing can be practiced regularly when in contact with patients or other products. Also considering the risk to health care workers proper use of protective equipments must be used by these professionals to avoid infection [4]. Lastly, the accessibility to various fields through internet, media, news etc. has made it possible for everyone to share and exchange information. This can lead to formulation and spread of incorrect news and thereby initiate a panic situation. This should be avoided for the betterment of the society and the accurate/right use of telecommunication must be implemented.

Conclusions

It has to be taken into consideration that there is still limited knowledge and research with respect to COVID-19 related health crisis. A number of studies and research are being carried out for as much enhancement of knowledgement for control of this viral infection and betterment of human life. Studies have reported that COVID-19 has caused immense damage in all aspects as compared to SARS-CoV and MERS-CoV. In order to study the potential vaccinations, antibodies productions are under research. One such study was carried out to investigate the binding of spike proteins in COVID-19 infection [22]. Studies in the past health outbreaks also have been carried out to study the potential binding of viral proteins to specific antibodies in order to find out [23]. Also, research to study the transcription and replication of viral RNA have been carried out previously [24]. The only means of controlling this infection spread is by following social distancing and maintaining self-isolation. This can be done by promptly following all the protocols imposed by the government globally. For this, a powerful prevention scrutiny is necessary for infection control. Adequate amount of appropriate nutritional diet, symptomatic therapy, and antiviral drug prescription are certain vital interventional procedures to be taken into account. Also as the old age group, immunocompromised, new born and patients with secondary debilitating diseases are at high risk, special care must be taken to prevent them. Taking into consideration that this is a pandemic disease all the necessary measure must be followed by every individual strictly. A small step towards preventing this pandemic by self-realization and following self-hygiene at home and work place will work magic overall. The connecting link to control spread of COVID-19 starts from home, society, state, country and the world as a whole. Research studies are the call of the hour and need of today for control of this viral infection.

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Conflict of Interest

No conflict of interest.

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