

Review Article

SYSTEMATIC REVIEW ON MECHANISM OF ACTION, MORTALITIES, MORBIDITIES, AND PREVENTION FROM COVID-19

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ABSTRACT: Coronaviruses are enveloped, positive-sense, single-stranded RNA viruses which belong to family *Coronaviridae*. These viruses are responsible for mild to severe respiratory ailments such as common cold to SARS, MERS and COVID-19. Pandemic COVID-19 is an ongoing issue of 2020. It starts from Wuhan city of China that later extended to the whole world (203 countries). However, according to another report of World Health Organization (WHO) the virus may start from some other part of the world rather than Wuhan city of China. The major structural components of COVID-19 are spike, envelope and nucleocapsid proteins. It enters the cell via cellular receptors angiotensin-converting enzyme 2 (ACE-2). Its symptoms are high fever, dry cough, fatigue, dyspnea, tiredness, headache, body-aches, pneumonia, and difficult breathing. Its man to man transmission is extraordinarily high and has ability to infect all age groups however, morbidity cases are noticed higher in elderly group of people. It can be transferred by the carriers via cough, sneeze or when they touched the surfaces or any object. It is concluded that there are more chances for the spread of disease in casual and workplaces. To control pandemic COVID-19 there is need to spread awareness about its structure, way of transmission and prevention. The present review discusses structure, mechanism of action, incubation period, most affected age groups, symptoms, transmission, and precautions to stop its progress.

Key words: Pandemic, morbidity, incubation, symptoms, transmission.

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INTRODUCTION

COVID-19 and its structure: The virus originated in Wuhan, China, is responsible for Severe Acute Respiratory Syndrome Coronavirus 2 and disease caused by it has been named as COVID-19 by the WHO. It is a member of beta-coronaviruses and has shown 70% resemblance in genetic sequence to SARS Coronavirus (Hui *et al.*, 2020). COVID-19 is an addition to already existing list of six strains of human coronaviruses (Hui *et al.*, 2020; Woo, *et al.*, 2006). 229E and NL63 are strains of Human Corona viruses that belong to *Alpha-coronaviruses* while OC43, HKU1, SARS, MERS, and COVID-19 are Human Corona viruses strains which belong to *Beta-coronaviruses* (Elfiky *et al.*, 2017; Elfiky, 2020). Its major components are spike, envelope and nucleocapsid proteins (Fig. 1). Polyclonal and monoclonal antibodies are also prepared against them (<https://www.prosci-inc.com/covid-19/>).

Mechanism action of COVID-19: Shereen *et al.*, (2020) reported mechanism of action of COVID-19 as the S proteins bind to the cellular receptor of angiotensin-converting enzyme 2 (ACE-2). Then, a conformational change in S protein facilitates viral envelope fusion with the cell membrane through the endosomal pathway. Later

on, release of RNA of COVID-19 into the host cell, starts translation and ultimately production of replicate polyproteins. The formation of series of sub-genomic mRNAs are finally translated into viral proteins. These synthesized viral proteins and genomic RNA join in the Endoplasmic reticulum and Golgi bodies to form virions (Fig. 2).

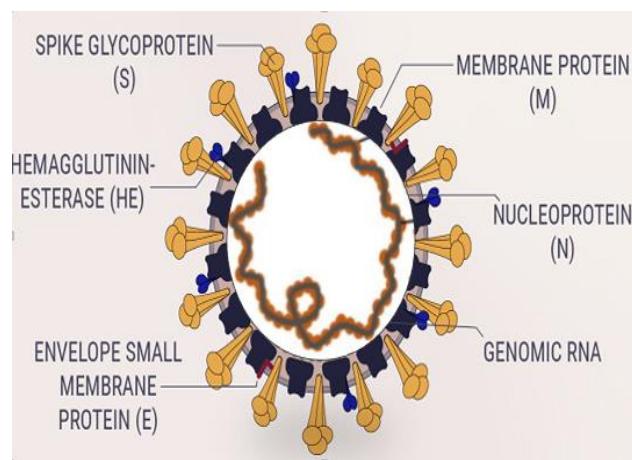
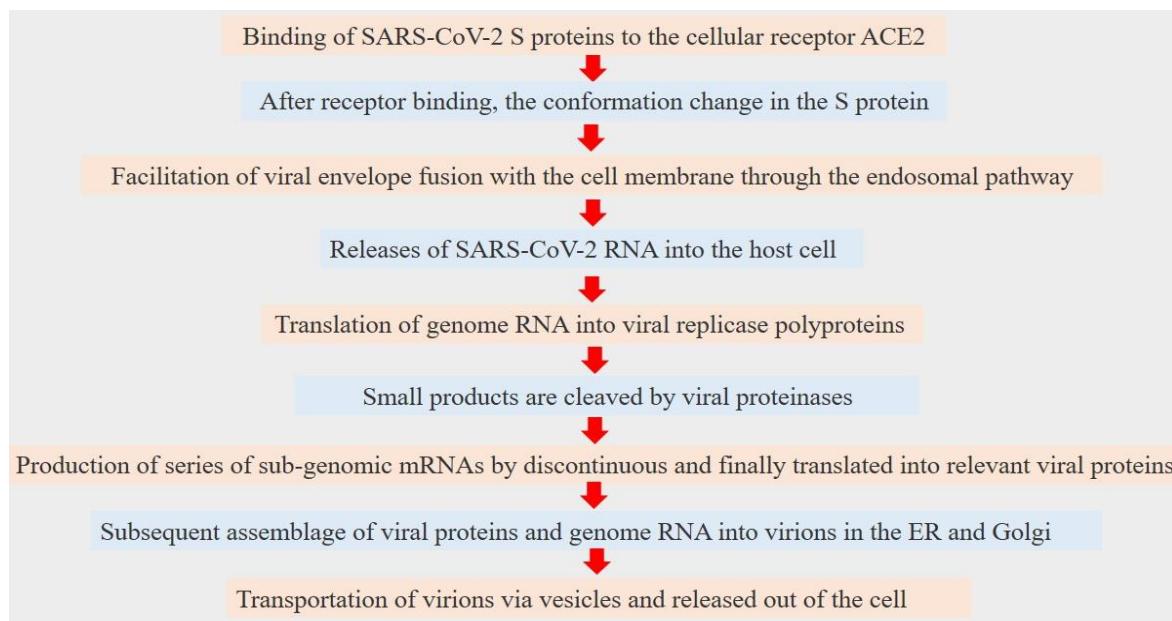


Fig. 1: Structure of COVID-19
(<https://reference.medscape.com/viewarticle/924391>)



Abbreviations: ACE-2, angiotensin-converting enzyme 2; ER, endoplasmic Reticulum

Fig. 2: Different steps from entry to exit in the life cycle of SARS-CoV-2 in host cells

Ultimately, transportation of virions takes place via the vesicles or outside the cells to infect more cells. Yan *et al.* (2020) also agreed that ACE-2 are the cellular receptors for SARS corona viruses and the novel strain COVID-19 epidemics.

Transmission and relation of infection with age: It is highly contagious and man to man transfer is high (Casella *et al.*, 2020). Man to man transfer occurs via air droplets, sneezing, cough, and contacts with living or non-living surfaces (Wu *et al.*, 2020; Heymann and Shindo, 2020). It was started in Wuhan, city China in December, 2019 and outbreak affects the whole world (Shi *et al.*, 2020; Mao *et al.*, 2020; Surveillances, 2020) Approximately, in 199 countries, total confirmed cases of pandemic COVID-19 on 29th March were 710,950 with 33, 553 deaths and 150, 734 recoveries. (<https://www.worldometers.info/coronavirus/#countries>). COVID-19 transmission is possible even with the asymptomatic carriers and may pose serious public health impacts (Al-Tawfiq *et al.*, 2020; Bai *et al.*, 2020). Results of a study that was carried out on a cruise ship showed its progression rate is very high as 10 initial cases were reported from 3700 passengers on 3rd Feb 2020 that reached to 619 by 20th of the February, 2020. Even isolation of ill passengers was implemented from 4th February, 2020 (Rocklov *et al.*, 2020). This COVID-19 virus has ability to infect people of all ages. However, evidence to date proposes that two categories of people are in a higher danger for receiving severe COVID-19 disease. These are old people (age over 60 years); and those which are already suffering from some medical problem (such as people with cardiovascular disease,

diabetes, acute or chronic respiratory disease, and some sort of cancer). It showed that risk to getting infected slowly increased with the age especially those which are around 40 years. It is necessary that people in this age range (40 -70) care for themselves and in turn protect others that may be impuissant (Novel, 2020). Wang and Zhang, (2020) determined in a cohort with COVID-19 in population of china that patients with cancer were more likely to develop this disease. However, from 18 patients out of 1590 confirmed cases of COVID-19 reported from 575 hospital of 31 provinces of China had cancer histories. Although, 12 out of 18 were recovered from initial cancer treatments showed there is no association of COVID-19 with the cancer patients. Shi *et al.*, (2020) reported results of a study in which 81 COVID-19 patients admitted in a hospital. Gender wise division of cohort showed 42 were men and 39 were women while with the average age of 49.5 years (SD 11.0. Similarly, in another study a total of 72, 314 patients were recorded with 61.8% confirmed cases that found within range of 30-79 years (Surveillances, 2020). In another study almost 87% patients were found between 30-79 years of age, 3% were aged 80 years or older. While, 1% were between 10-19 years of age, and only 1% were with age 9 or younger than nine (Wu and McGoogan, 2020). However, Qiu *et al.*, (2020) reported 36 children with average age of 8.3 years were found infected with COVID-19. Isolation of live COVID-19 from stool samples of an infected patient in China, confirmed that the virus has an alternate route to transmit (digestive system) other than respiratory system. Presence of COVID-19 nucleic acid in the stool and respiratory samples was first reported in one of the USA infected

patient (Gu *et al.*, 2020; Lescure *et al.*, 2020). Moreover, faecal-oral transmission of COVID-19 is now supported by number of studies (Hindson, 2020; Yeo *et al.*, 2020). Although, a lot of research is going about this virus in different infected people. However, presently, no data is available that showed transmission of COVID-19 transplacentally from mother to the newborn (Lu and Shi, 2020).

Incubation period of COVID-19: There are more or less variations in incubation period of COVID-19 reported in literature. As according to Shi *et al.*, (2020) and Wu *et al.*, (2020) average incubation period of COVID-19 recorded as 6.4 days with basic reproduction number ranged 2.24 to 3.58 days. While, Lai *et al.* (2020), reported incubation period 2-14 days and Lauer *et al.* 2020 gave median value for incubation period as 5.1 days. Tian *et al.*, (2020) evidenced a study in Beijing and reports a median incubation period as 6.7 days while, the interval time from between illness onset and visiting a doctor was 4.5 days. Incubation period of 3 days (0-24 days range, study based on 1,324 cases) and 5.2 days (4.1-7.0 days range, based on 425 cases) was also mentioned on this link (<https://www.worldometers.info/coronavirus/coronavirus-incubation-period/>).

COVID-19 Diagnostic Methods: For the diagnosis of COVID-19 different methods are in practice which includes CT, nucleic acid testing, throat swab, Anal swab. A single most authentic technique is not still finalized however, Computed Topography (CT) is in use for investigation from the start of the disease as it helps to identify disease severity and recovery and can also differentiate diverse stages of the disease (Harahwa *et al.*, 2020). Similarly, the use of a nucleic acid-based test such as the reverse-transcriptase polymerase chain reaction (RT-PCR) has proven to be helpful in direct confirmation of COVID-19 infection (Harahwa *et al.*, 2020). According to report of Wu *et al.* (2020) the CT sensitivity was recorded as 97.2%, while sensitivity to the first rRT-PCR was found 83.3%. It was all reported that all the COVID-19 diagnostic methods have their own limitations (Kumar *et al.*, 2020). Previous studies have shown positive testing of RT-PCR in the throat swabs of patients diagnosed with COVID-19, which led to a conflict with clinically cured cases that had only positive effects on anal swabs. This contradicted the current practice of discharge, and continued to investigate the clinical value of anal swabs for the acquisition of COVID-19. It is proposed anal swabs as a viable example of COVID-19 acquisition testing for hospital discharge of patients (Lan *et al.*, 2020; Sun *et al.*, 2020). There is still a debate is going about different diagnosis methods and their reliability which can be proven fruitful with the further research studies regarding this field.

COVID-19 Symptoms of morbidities: Most commonly reported symptoms were noticed as high fever (38.5 °C), dry cough, fatigue, dyspnea, headache, acute upper respiratory symptoms, and pneumonia (Tian *et al.*, 2020; Qiu *et al.*, 2020; Xu *et al.*, 2020). In addition to all these, consolidation, bilateral and peripheral disease in lungs were reported with Computed Topography (CT) (Bernheim, *et al.*, 2020). Similarly, presence of diarrhea, nausea and vomiting also noted in COVID-19 patients. However, autopsy studies was required to understand presence of COVID-19 in the digestive system and it is evidenced with autopsy of single patient (85 years old) that showed segmental dilations and stenosis in the small intestine. Although, pre-existing effect of ailment in this case was not known (Mao *et al.*, 2020).

Rate of Mortalities due to COVID-19 in few countries: COVID-19 has been proven very fatal since the first case reported in Wuhan, City (China) in December, 2020 (Lim *et al.*, 2020; Wu *et al.*, 2020). However, this acute respiratory disease transmits within 3 months to 203 countries and based on World Health Organization (WHO) reports, total confirmed cases of pandemic COVID-19 on 1st April were 860,178 with 42, 344 deaths and 178, 442 recoveries. Some literatures states that it may start in other places even before outbreak in Wuhan however, some more research is required to find its original source (<https://www.bbc.com/news/world-asia-china-55996728>). The mortality rate was reported highest for Italy followed by Spain, United States, China, France, Iran, United Kingdom, Netherlands, and Germany as shown in (Fig. 3).

Treatment of COVID-19: It was noticed that during the treatment of 36 infected children from COVID-19 that twice use of interferon- α by aerosolization remained effective. Even though, some children received lopinavir-ritonavir syrup twice a day and some were also provided oxygen to inhale. All children were cured from this disease and discharged within 14 days (Qiu *et al.*, 2020). While, Cao *et al.*, (2020) reported about adult patients which were hospitalized due to COVID-19, no benefits were recorded with lopinavir-ritonavir treatment beyond standard care. Similarly, Hydroxychloroquine treatment results were noticed in a small group and it was significantly related to reduce viral load and vanishing COVID-19 in patients. Moreover, effects of Hydroxychloroquine were reinforced by Azithromycin (Gautret *et al.*, 2020). Various studies reported that Chloroquine was found effective to control COVID-19 (Colson *et al.*, 2020; Cortegiani *et al.*, 2020; Devaux *et al.*, 2020; Negahdaripour *et al.*, 2020; Touret *et al.*, 2020). Chloroquine and Hydroxychloroquine, both were found effective in treatment of COVID-19 (Singh *et al.*, 2020). In one more study, Chloroquine phosphate that was an old antimalarial drug, has shown efficacy to treat COVID-19 cases. Supply of oxygen and extracorporeal

membrane oxygenation for the mild cases and critically ill patients were also useful in COVID-19. Convalescent plasma or immunoglobulins remedy was also found effective (Chen *et al.*, 2020). Remdesivir was found superior to placebo in shortening the time to recovery in

adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection (Beigel *et al.*, 2020). Viral load in the blood plasma can be reduced by sonication as reported in a study by Pforringer *et al.*, (2020).

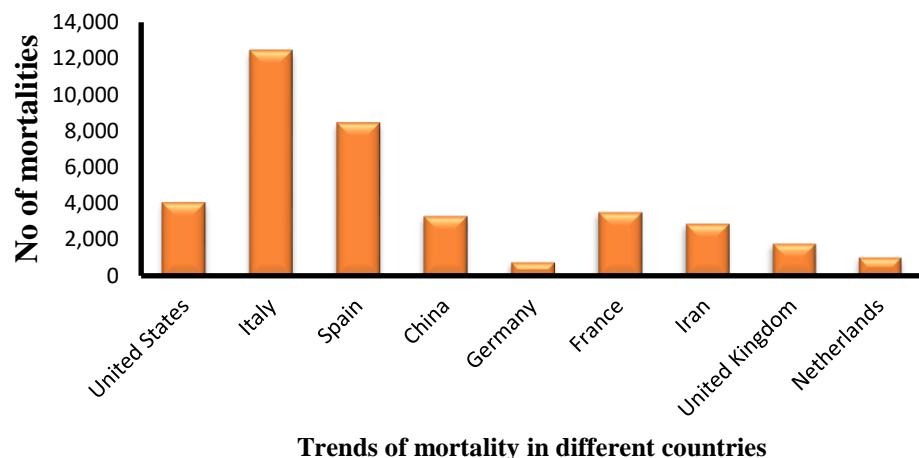


Fig. 3: Number of mortalities in different countries

Prevention for the control of COVID-19: To control outbreaks of COVID-19, isolation and contact reduction is required. Its epidemic transmission can be controlled well if patients were isolated early to avoid close contact with families and communities (Hellewell *et al.*, 2020; Tian *et al.*, 2020). According to Rothan and Byrareddy, (2020) special attention and struggles should be required to protect and reduce transmission of COVID-19 in susceptible population such as children, elderly people, and health care providers. So, restrictions in travelling to and from China worked well with reductions in community contact (Chinazzi *et al.*, 2020). The Chinese Government has taken some immediate steps to control COVID-19 such as closure of schools (almost 220 million children and adults were confined to their homes), discouraging of the public activities. According to Chinese Ministry of Education, 180 million (both from primary and secondary schools) and 47 million (Preschool students) were kept at home during the outbreak. During lockdown, schools and teachers remained efficient and worked well through virtual education system and online courses were taught via television broadcasts and internet (Wang *et al.*, 2020). Moreover, quarantine, public distancing, and inaccessibility of infected people can hold the widespread of COVID-19 very well in China and encouraged other countries like Pakistan to reduce impact of this disease by strict compliance of the rules (Anderson *et al.*, 2020). Similarly, various countries in Africa are pacing up and made the public attentive against pandemic COVID-19 by increased surveillance, resources, and capacity

building (Gilbert *et al.*, 2020). Moreover, regular washing of hands, maintenance of safe distance, frequent use of sanitizers, use of steam and drinking of boiled water are encouraged. Improvement of immunity due to use of nutrient rich diet with vitamins A, B, C, D and E and minerals (Selenium, Zinc, Iron,), Ω -3 polyunsaturated fatty acids and immune-enhancers are also helpful to cure this disease (Zhang and Liu, 2020).

Conclusion: COVID-19 has been proven as one of fatal human coronavirus whose transmission is possible both through faecal-oral contacts. The outbreak can be controlled by isolation, quarantine, less public contact and as in China, it was only controlled by implementing severe lockdown. However, for developing countries like Pakistan where public awareness should be needed, electronic and social media (Facebook, WhatsApp, television, and newspaper) can be quite helpful. If they work with the Government to guide people about this epidemic and aware the public about benefits to comply and adhere to strict rules and regulations.

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