

A comprehensive review: Coronavirus disease 2019 (COVID-19)

¹Rohit Pal, ²Ghanshyam Teli, ³Harendra Bisht

Pharmaceutical Chemistry,

^{1,2}ISF College of Pharmacy, Moga, India

³Kumaun University Nanital, India

Abstract: In March 2020 the World Health Organization described the SARS-Cov-2 virus as global pandemic. In the whole world, confirmed cases and death rate are increasing in exponential way. SARS-Cov-2 belong to the genus Coronavirus with its high mutation rate in the Coronaviridae. The strain probably in bats and it is zoonotic but human-to-human transmission is also possible. The disease is transmitted by contact with infected droplets or inhalation and the incubation period may ranges from 2 to 14 days. The symptoms usually include fever, sore throat, cough, breathlessness, fatigue, malaise among others. In most people the diseases are mild; whereas some (usually the elderly and those with comorbidities), it may progress to pneumonia, acute respiratory distress syndrome (ARDS) and multi organ dysfunction. Many people are asymptomatic. Treatment is essentially supportive; role of antiviral agents is yet to be established. Antiviral regimen or combination of hydroxychloroquine with azithromycin has shown positive results. This review highlights a picture of the current status on public health impact, pathophysiology and clinical manifestations, diagnosis, case management, emergency response and preparedness.

Keywords: SARS-Cov-2, Combination, Treatment, Strain, Asymptomatic, Pandemic.

I. INTRODUCTION

The COVID-19 outbreak was declared as was declared a pandemic by the World Health Organization (WHO) on March 11, 2020 [1]. The whole world is doing intensive effort to establish effective treatments and develop a vaccine for the disease. WHO named this disease as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and it belongs to the family of the pathogen that is responsible for respiratory illness linked to the 2002–2003 outbreak (SARS-CoV-1) [2]. To protect under this pandemic, there is an urge to manufacture a greater number of respirators and masks to prevent any aerosol with microbes. To reduce the transmission, WHO suggest to use the personal respiratory protective equipment. The virus has natural and zoonotic origin and the clinical feature are variable. The risk factors are highly variable and making the clinical severity range from asymptomatic to fatal [3]. This review summarizes the details of prevention, virology, various diagnostic method and mode of transmission of the COVID-19. The aim of the review to peer on the sign and symptoms and various treatment being used to treat the infection.

II. HISTORY

The Chinese population was infected with a virus in 2003 causing Severe Acute Respiratory Syndrome (SARS) in Guangdong province. The virus was identified as a member of β -Coronavirus and was named SARS-CoV. The origin of SARS-CoV in bats transmitted to humans via palm civet cats in the Guangdong province of china. Because of SARS-CoV more than 8000 people were affected in China and Hong kong and caused 916 deaths (mortality rate 11%) [4].

A decade later in 2012, a couple of Saudi Arabian were diagnosed to be infected with another coronavirus. The identified virus was confirmed as a member of coronaviruses and named as the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The MERS-CoV was also originated from bats and due to this 2494 people was infected and caused 858 deaths (Mortality rate 34%) [5].

Recently, In December 2019, a group of pneumonia cases, caused by a newly detected β -Coronavirus occurred in Wuhan, China. The virus was named as the 2019-novel Coronavirus (2019-nCoV) on 12 January 2020 by World Health Organization (WHO) and The disease was officially named as coronavirus disease 2019 (COVID-19) by WHO and Coronavirus study group (CSG) of the International committee proposed to name the new coronavirus as SARS-CoV-2, both issued on 11 February 2020. The Chinese scientists was rapidly isolated the coronavirus from a patient within a short time on 7 January 2020 and then identified the genomic sequence of the SARS-CoV-2[6]. As of 23 Aug 2020, a total of 22,812,491 cases of covid-19 have been confirmed in the world including 7,95,132 deaths (Mortality rate is 3.49%) [7].

III. EPIDEMIOLOGY

All age groups are susceptible to the infection. Through large droplets generated during coughing and sneezing by symptomatic patients but can also occur from asymptomatic people and before onset of symptoms the infection is transmitted [8]. The various studies have shown that higher viral batches are present in the nasal cavity in as compared to the throat with no difference in viral burden between symptomatic and asymptomatic people. As long as for as the symptoms last and even on clinical recovery the patients can be infectious. Some people may act as super spreaders; a UK citizen who attended a conference in Singapore infected 11 other people while staying in a resort in the French Alps and upon return to the UK. These infected droplets can deposit on surfaces and can spread 1–2 m [9]. The virus can remain viable and can live on surfaces for days if suited atmospheric conditions is provided but are destroyed easily in less than a minute by use of common disinfectants such as sodium hypochlorite, hydrogen peroxide etc. either by inhalation of these droplets or touching surfaces contaminate and then touching the eye, mouth and nose, the infection is acquired [10,11]. The studies also show that the virus is also present in the stool and contamination of the water supply and subsequent

transmission via aerosolization/ feco oral route is also hypothesized. As per latest information, transplacental transmission are not occur i.e., from pregnant women to their fetus has not been described. However, neonatal disease can be prevailed i.e., due to postnatal transmission is described [11]. The incubation period varies from 2 to 14 days [median 5 d]. Studies have also reported that angiotensin receptor 2 (ACE2) is the through which the virus enters the respiratory mucosa [12]. In various modelling studies the basic case reproduction rate (BCR) is estimated to range from 2 to 6.47.

IV. PATHOGENESIS-VIROLOGY

The COVID-19 contain the genome structure RNA i.e., the best to all RNA viruses. It contains the largest known RNA genomes—30–32 kb—with a 50-cap structure and 30-poly-A tail, in which two-third of its RNA is encoded by viral polymerase (RdRp). The other part i.e., one-third of the genome encodes four structural proteins (spike (S), envelope (E), membrane (M) ve nucleocapsid (N), and the other helper proteins.[9,13] According to the studies, it has been realized that the viral RNA synthesis of polyprotein 1a/1ab (pp1a/pp1ab) is take place in the host. The transcription performed through the replication-transcription complex (RCT) and which is assemble in double-membrane vesicles and through the synthesis of sub genomic RNAs (sgRNAs) sequences. On next the transcription termination carries at transcription regulatory sequences which is located between the self-titled open reading frames (ORFs) that functions as templates for the synthesis of sub genomic mRNAs. At least minimum six ORFs can be present, in the atypical CoV genome. During these frame shift among ORF1a and ORF1b guides the synthesis of both pp1a and pp1ab polypeptides which are poised by virally encoded chymotrypsin-like protease (3CLpro) or main protease (Mpro), moreover one or two papain-like proteases are also poised for producing 16 non-structural proteins (nsps) [10]. There are other also ORFs present which are encode for structural proteins and include spike, membrane, envelope, and nucleocapsid proteins and accessory proteic chains, apart from ORF1a and ORF1b [10,11]. Different CoVs are present with special structural and accessory proteins which are translated by committed sgRNAs [14].

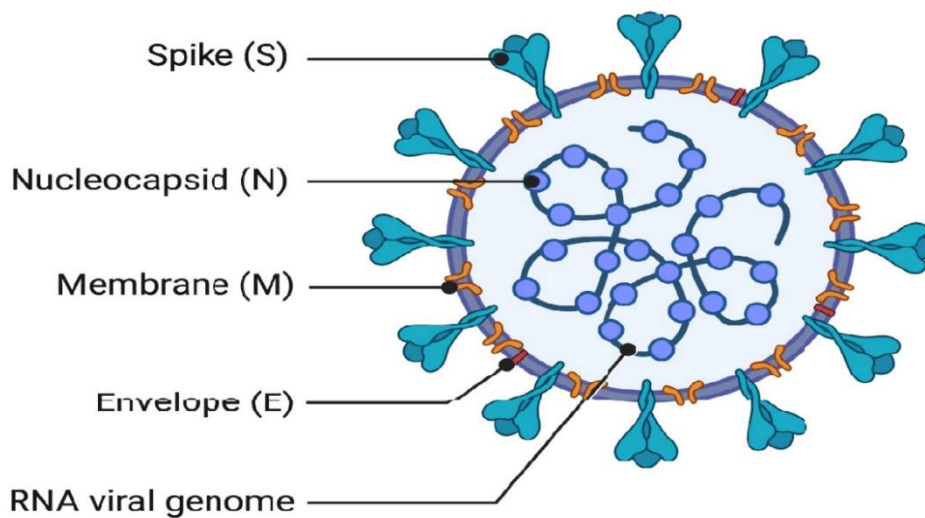


Figure 1 Genomic structure of coronavirus

Pathogenesis and virulence mechanisms of CoVs and thus also of SARS-CoV2 have explain by association to the function of the nsps and structural proteins. For note, research has highlight that nsps are skilled to block the host innate immune response [12]. In all the functions of the structural proteins, envelope possess the vital role in the virus pathogenicity because it promotes release and viral assembly.

After various studies, the observation concludes that the pathogenic mechanism that produces pneumonia looks to be particularly complex [11,12]. The data till now available looks to define that viral infection is skillful of generating an excessive immune reaction in the host. In some of the cases, a reaction occurs, which all in all is stamp a “cytokine storm”. The consequence is ample tissue damage. The interleukin 6 (IL-6) play as the protagonist of cytokine storm. IL-6 is generated by activated leukocytes and make a move on a large number of cells and tissues [14]. It is apt to foster the differentiation of B lymphocytes, inhibits the growth of some categories of cells and promotes the growth of some others. It also revives the production of acute phase proteins and plays a supreme role in bone maintenance, in thermoregulation and in the functionality of the central nervous system [15]. Although the important role played by IL-6 is pro-inflammatory, it can also have anti-inflammatory effects. On the other hand, IL-6 increases during inflammatory diseases, autoimmune disorders, cardiovascular diseases, infections, and some types of cancer [16].

The first step include that the virus might pass via the mucous membranes, especially via nasal and larynx mucosa, after that secondly enters the lungs via the respiratory tract. On the third step the virus likely to attack the targeting organs, such as the lungs, heart, renal system and gastrointestinal tract that express angiotensin converting enzyme 2 (ACE2) [15,17]. on the next step virus begins a second attack, causing the patient’s condition to aggravate around 7 to 14 days after onset. Afterword B lymphocyte decrease may occur early in the disease, which may result to affect antibody production in the patient. Besides, the inflammatory factors associated with diseases mainly containing IL-6 were significantly increased, which also contributed to the aggravation of the disease around 2 to 10 days after onset.

The clinical spectrum of COVID-19 varies from paucisymptomatic or asymptomatic and results to forms clinical conditions which are characterized by severe respiratory failure that necessitates mechanical ventilation and support in an intensive care unit (ICU), to multiorgan and systemic manifestations in terms of septic shock, sepsis, and multiple organ dysfunction syndromes (MODS)[18]. Asymptomatic infections have also been recorded and using best of knowledge has been described, but making a note that the frequency is unknown. The principal symptoms are reported in **Table 1**. The serious manifestation of infection that appears to be the most frequent is pneumonia, which is characterized primarily by fever, cough, bilateral infiltrates on chest imaging and dyspnea. [19] There are no distinct clinical features that can yet accurately discriminate between other viral respiratory infections and COVID-19. Some, less minor common symptoms have embraced, sore throat, headaches, and rhinorrhea. In various researches gastrointestinal symptoms such as nausea and diarrhea have also been reported in addition to respiratory symptoms. Respiratory droplet transmission is the main route and it can also be transmitted through person-to-person contacts by asymptomatic carriers [18,19].

Table 1 Main COVID-19-associated symptoms.

S.NO.	SYMPTOMS
1.	Fever
2.	Cough
3.	Dyspnea
4.	Sore throat
5.	Head ach
6.	Rhinorrhea

V. TRANSMISSION

The definition of novel corona virus from various studies can elucidate as a novel respiratory tract virus which causes coronavirus disease 19 (COVID-19). It is highly transmittable and pathogenic infection. The primely the transmission occurs through the respiratory droplets, when the infected person sneezes or cough. About 3,000 droplets circulates on a single cough [20]. These droplets can settle down on other people, and covering surfaces around them, however, several smaller particles will stay within the air. Therefore, it can be said that it is transmitted through human to human [21,22].

It has been also investigated that SARS-CoV-2 can be viable on aerosols (produced via a nebulizer) for at least 3 hours. according to WHO evaluation the reproductive number (R0) of COVID-19 is 1.4 to 2.5. However, some other studies also evaluate and estimate R0 of 3.28 [23]. The virus is also spread through the fecal matter by shedding from it, thus anyone who not washing their hands thoroughly after visiting the toilet, bathroom could contaminate anything they touch like many respiratory viruses, including flu, Covid-19 can be spread by close contact with small droplets released from infected individuals' upper respiratory tract secretions,[21] e.g. sneezing, common cold or coughing from the nose and mouth. That is why WHO suggested, to stay more than 1 meter (3 feet) away from a person who is sick.

The virus can be spread through surface contamination when these droplets sets on surfaces and objects like door handles, pen, railings, walls, glass etc, the person around and other individual touches these surfaces or objects and further touching their mouth, eyes or nose then these people can catch COVID-19 and feel sick. The studies have reported that the novel virus causing epidemics coincides with the CoV isolated in bats. This is evaluated by the analysis of genetic tree of virus, but whether the virus jumped directly from bats or whether there was an intermediary animal host is not known yet [23] The transmission of COVID-19 is depicted in the figure

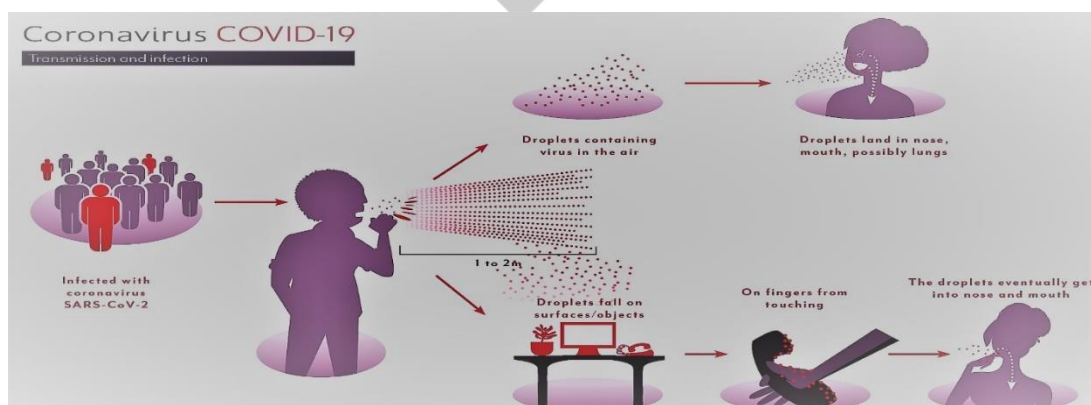


Figure 2 Mode of transmission of coronavirus

Corona virus can mutate effectively, which made this virus highly contagious. The studies data results that one infected person generally infects two to three others, which would make the new coronavirus more contagious as compare to other coronaviruses,

like SARS and MERS. To prevent such transmission, people should stay at home and rest while symptoms are active and also one should also avoid close contact with other people as to prevent further transmission. The transmission can also be prevented by covering the mouth and nose with a tissue or handkerchief while coughing or sneezing. It is important to dispose of any such tissues after use and maintain hygiene around the home and the environment.

VI. TYPE OF CORONA VIRUS

CoVs is novel respiratory virus. This contains the large family of virus which are very common in different animal species which includes camels, cattle, cats, and bats. They can cause diseases ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). Rarely, animal CoVs can infect humans and, as a result, may spread among humans during epidemics such as MERS, SARS, and COVID-19 [9-12]. The subfamily from which it belongs to is Coronavirinae in the family Coronaviridae. The various researcher and Doctors currently recognize that there are seven types of coronavirus that can infect humans, that are listed below: -

1. 229E (alpha coronavirus)
2. NL63 (alpha coronavirus)
3. OC43 (beta coronavirus)
4. HKU1 (beta coronavirus)
5. MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS)
6. SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS)
7. SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19) [21, 22].

VII. CORONA VIRUS LIFE CYCLE

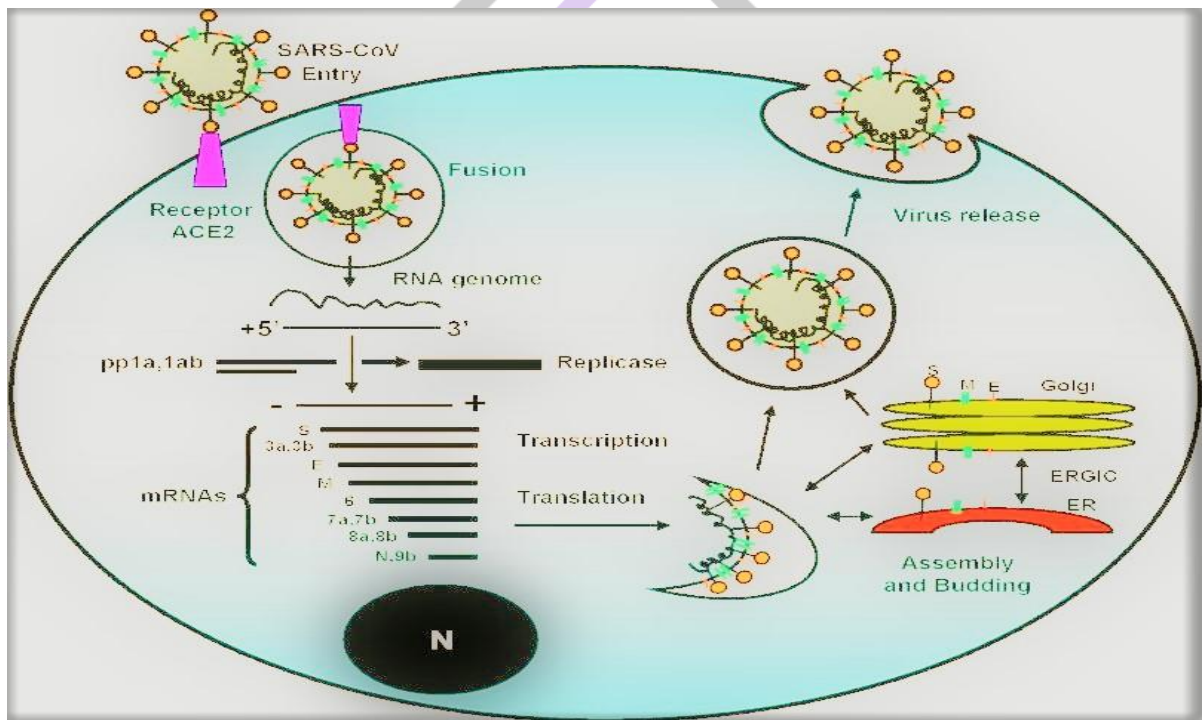
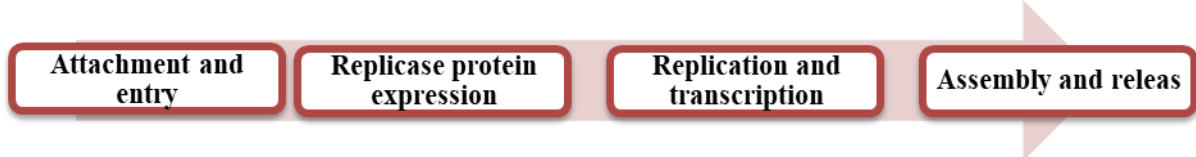


Figure 3 Stages of Coronavirus Life Cycle

There are the following in the life cycle of COVID-19 virus: -



VIII. SYMPTOMS

Cold- or flu-like symptoms experienced by maximum patients infected with the virus, usually set in from 2–4 days. Some of the patients infected with the virus do not experience such symptoms i.e., asymptomatic. About 80% of patients experienced mild symptoms of diseases. Studies shows that most of the adults have the best immunity which can fight against the infection but they are more likely to spread the infection which accounts the disadvantageous. However, symptoms may vary from person to person. According to the studies WHO classify the stages of severity and different percentage of people comes under the severity [24,25,26].

S.NO.	STAGE OF SEVERITY	ROUGH PERCENTAGE OF PEOPLE WITH COVID-19
1.	Mild disease from which a person can recover	More than 80%
2.	Severe disease, causing breathlessness and pneumonia	Around 14%
3.	Critical disease, including septic shock, respiratory failure, and the failure of more than one organ	About 5%
4.	Fatal disease	2%

The various symptoms include with the new coronavirus are: -

1. Sneezing
 2. Runny nose
 3. Cough
 4. Watery diarrhea
 5. Fever in rare cases
 6. Sore Throat
 7. Exacerbated asthma
- The symptoms seem to start with fever, followed by fatigue, muscle pain and dry cough.
 - After a week, Patients may suffer from shortness of breath with breathing problem especially if they are elderly or have some pre-existing health condition. The COVID-19 symptoms are similar to some of the influenza and respiratory infections i.e., fever, cough and shortness of breath.
 - By the end of the first week patients can develop pneumonia which ultimately results into acute respiratory distress syndrome (ARDS), a condition where the fluid fills up in the lungs and this is mostly fatal. This mostly happens in severe cases.
 - The progression of diseases accounts to worsening of symptoms, which ultimately leads to the point where immediate requirement for ICU is necessary [27, 28].
 - At the time of mild condition patients, may suffer probably with more abdominal pain and loss of appetite.
 - In the 2nd or 3rd wee the recovery of the patients starts.
 - 10 days is the median duration for the hospitalization who recovered from the diseases.

However, it is difficult to identify the symptoms in earlier days of the diseases. According to the reports the symptoms spectrum ranges from mild to severe range [20, 29].

IX. INCUBATION PERIOD

According to the studies, the incubation periods accounts from 2-14 days. Some of the reports also accounts the incubation periods for 24 days which is contrasts to the previous studies. Some of the studies also accounts the incubation periods for 88 days among confirmed cases in china. These data suggest the more extended quarantine period [20, 21, 22, 42, 48].

X. PREVENTION AND PRECAUTION

There are several properties of this virus make preventive measures difficult such as, the infectivity even before onset of symptoms in the incubation period, non-specific features of the disease, long incubation period, transmission from asymptomatic people, tropism for mucosal surfaces such as the conjunctiva, transmission even after clinical recovery and prolonged duration of the illness[30]. Therefore people should stay aware of the current information on the COVID-19 outbreak provided by WHO and should follow the directions of your local health authority and prevent secondary infections, interrupt human-to-human transmission to your close contacts health care workers and prevent further spread [31].

The most people who are infected with COVID-19 encounter mild illness and recover it, but its infection can be more severe for other individuals. One should take care health and protect others [32].

The succeeding steps should be followed for the prevention: -

Hand hygiene

- hand hygiene comprises either cleansing hands with soap and water for at least 20 seconds or with an alcohol-based hand rub (ABHR) (hand sanitizer that contains at least 60% alcohol);
- if hands are not visibly soiled, alcohol-based hand rubs are preferred;
- when they are visibly soiled, wash hands with soap and water [33].

Respiratory hygiene

- Respiratory hygiene comprises that all patient should cover their nose and mouth with a tissue or elbow when coughing or sneezing;
- offer a medical mask to patients with suspected 2019-nCoV infection while they are in waiting/public areas or in cohosting rooms;
- perform hand hygiene after contact with respiratory secretions.

- It is compulsion for everyone to wear face mask while at public place or at work place, where there are chance for transmission of the infection [34].

Social distancing

- When infected individuals cough or sneezes, they spray small droplets from their nose or mouth which may contain COVID-19 virus. The person can breathe in these droplets.
- Therefore, maintain social distancing (maintain at least 1 meter or 3 feet distance between yourself and anyone)
- avoid close contact with people who are sick (who is coughing or sneezing).
- Avoid large events and mass gatherings [35].

Use of PPE

The cogent and veracious use of PPE reduces exposure to pathogens. The effectiveness of PPE strongly depends on:

- staff training on putting on and removing PPE;
- prompt access to sufficient supplies;
- appropriate hand hygiene;
- health worker compliance;
- regular monitoring and feedback by IPC personnel [36].

Environmental cleaning

It is vital to clinch that cleaning and disinfection procedures are followed consistently and correctly. All surfaces in health-care facilities and work places should be routinely cleaned and disinfected, especially high-touch surfaces, and whenever visibly soiled or if contaminated by body fluids [33, 37]. In areas where suspected or confirmed COVID-19 patients are admitted, frequency depends on type of patient areas and surfaces. Detailed guidance on environmental cleaning and disinfection in the context of COVID-19 is given by WHO [34].

- Surfaces are thoroughly clean with water and detergent;
- application of a disinfectant solution.
- For COVID-19, either 0.1% (1000ppm) sodium hypochlorite or 70-90% ethanol is effective.
- However, if there are large spills of blood or body fluids, a concentration of 0.5% (5000ppm) sodium hypochlorite should be used;
- the minimum contact time, 1 minute is recommended for ethanol, chlorine-based products and hydrogen peroxide $\geq 0.5\%$; 14 4) after appropriate contact time, disinfectant residue may be rinsed off with clean water if required [38, 39].
- Medical devices and equipment, laundry, food service utensils and medical waste should be managed in accordance with safe routine procedures [36, 40].

XI. DIAGNOSIS

The following diagnosis methods are used for the patient suspected with infection: -

1. **RT-PCR:** For the detection of infection real-time fluorescence (RT-PCR) can be utilized, help to detect the positive nucleic acid of SARS-CoV-2 in sputum, throat swabs, and secretions of the lower respiratory tract samples [41]. It is gold standard method for confirmation of infection [42]. preceded by RNA extraction from the nasopharyngeal and oropharyngeal secretions, followed by a reverse transcription step to convert RNA into complementary DNA (cDNA) that will undergo amplification [43, 44, 45].
2. **Laboratory methods:** The diagnosis of the covid-19 may include based on the based on the clinical and epidemiological history of the patient and it is generally nonspecific. The WBC count is usually normal or may low. There may be lymphopenia; a lymphocyte counts less than 1000 generally been found. The platelet count is usually normal or mildly low and in sever condition extremely low. The ESR and CPR are generally increased but procalcitonin levels are usually to normal level. A high procalcitonin level may indicate a bacterial co-infection. The ALT/AST, prothrombin time, creatinine, D-dimer, CPK and LDH may be elevated and high levels are associated with severe disease [43].
3. **Radiological examinations:** The radiological examination can be performed for the identification of corona infection. But the it is not sensitive in early stages as it cannot detect ground glass opacity (GGO) [46]. In sever patients, bilateral multifocal consolidation is partially fused into massive consolidation with small pleural effusions and even presenting with “white lung” [47].

XII. TREATMENT

Table 2 Inpatient Treatment Regimens

(1) Dual-drug regimen
The Proposed antiviral regimen for the treatment of hospitalized covid-19 cases includes:
Chloroquine/hydroxychloroquine + clotra (atazanavir/ritonavir) or (lopinavir/ritonavir)
(a) Two 250 mg chloroquine phosphate tablets or two 200 mg hydroxychloroquine sulfate tablets (equivalent to 150mg baseline) single dose (one dose)
(b) Clotra tablets (lopinavir/ritonavir) 200/50 mg every 12 hours two pcs for at least 5 days
The duration of treatment, depending on the clinical response of patient, can be increased to 14 days.
If the patient can't tolerate gastrointestinal complications, patients with a history of disorders of cardiac rhythm or high risk of drug interaction can use atazanavir/ritonavir instead of clotra (lopinavir/ritonavir)
Tablet (atazanavir/ritonavir) 300/100 mg: one daily tablet with food for at least 5 days.
If started (atazanavir/ritonavir), 200 mg twice daily (400 mg daily) of hydroxychloroquine will continue until the end of treatment
(2) The triple-drug regimen
If any of the following symptoms occur, severe illness should be considered: persistent hypoxemia, consciousness reduction, RR \geq 24 BP < 90/60, multilobular infiltration (CXR/CT scan) then hydroxychloroquine/chloroquine + clotra (atazanavir/ritonavir) or (lopinavir/ritonavir) + ribavirin
(a) Two 250 mg chloroquine phosphate tablets or two 200 mg hydroxychloroquine sulfate tablets (equivalent to 150 mg baseline) single dose (one dose)
(b) Clotra tablets (lopinavir/ritonavir) 200/50 mg every 12 hours two pcs for at least 5 days
(c) Ribavirin 1200 mg capsule/tablets every 12 hours (every 12 hours six pcs) for at least 5 days
The duration of treatment, depending on the clinical response of patient, can be increased to 14 days.
If the patient can't tolerate gastrointestinal complications, patients with a history of disorders of cardiac rhythm or high risk of drug interaction can use atazanavir/ritonavir instead of clotra (lopinavir/ritonavir)
Tablet (atazanavir/ritonavir) 300/100 mg: one daily tablet with food for at least 5 days.
If started (atazanavir/ritonavir), 200 mg twice daily (400 mg daily) of hydroxychloroquine will continue until the end of treatment
It is noted that the simultaneous administration of clotra and chloroquine can cause cardiac complications (like arrhythmia), so caution should be exercised in the regard

Table 3 Treatment of pregnant women with coronavirus

(1) Outpatient drug treatment for high-risk cases
This medical treatment can only be recommended for a pregnant mother who is at risk (with specific illness or immunodeficiency)
Two 250 mg chloroquine phosphate tablets or two 200 mg hydroxychloroquine sulfate tablets (equivalent to 150 mg baseline) single dose (one dose) every 12 hours for a minimum of 5 days.
(2) Double drug regimen
Two 250 mg chloroquine phosphate tablets or two 200 mg hydroxychloroquine sulfate tablets (equivalent to 150 mg baseline) single dose (one dose) every 12 hours for a minimum of 5 days.
Tablet (atazanavir/ritonavir) 300/100 mg: one daily tablet with food for at least 5 days or Clotra tablets (lopinavir/ritonavir) 200/50 mg every 12 hours two pcs for at least 5 days [49]

XIII. CONCLUSIONS

This review provides an insight into the COVID-19 current situation and represents a picture of the current state of the art in terms of public health impact, pathophysiology and clinical manifestations, diagnosis, case management, emergency response and preparedness. It is confirmed that for corona age doesn't matter as it is affecting people from all age group. Education about preventive measures and isolation and self-quarantine will also help debunk the load over the medical system. Moreover, strengthening of the public health system both medical and paramedical is the need of the hour. This review and current situation confirmed that a lot of work need to be done and it is one of the most thinkable situations for whole world to developed the vaccine.

REFERENCES

- [1] World Health Organization, Coronavirus disease (COVID-2019) situation reports. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>. Accessed 9 May 2020.
- [2] A. R. Fehr, S. Perlman, Coronaviruses: An overview of their replication and pathogenesis. *Methods Mol. Biol.* 1282, 1–23 (2015).
- [3] Buonsenso D, Piano A, Raffaelli F, Bonadia N, de Gaetano Donati K, Franceschi F. Point-of-Care Lung Ultrasound findings in novel coronavirus disease-19 pneumoniae: a case report and potential applications during COVID-19 outbreak. *Eur Rev Med Pharmacol Sci* 2020; 24: 2776-2780.
- [4] Chan-Yeung M, Xu RH. SARS: epidemiology. *Respirology*. 2003;8:S9–14.
- [5] Middle East Respiratory Syndrome Coronavirus. Available at: <https://www.who.int/emergencies/mers-cov/en/>. Accessed 16 Feb 2020.

- [6] Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020;395(10224):565–74.
- [7] WHO. Coronavirus disease (COVID-2019) Dashboard. 2020. <https://covid19.who.int/> Accessed 23 Aug 2020.
- [8] Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from and asymptomatic contact in Germany. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMc2001468>.
- [9] Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMoa2001316>.
- [10] Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents. *J Hosp Infect*. 2020 Feb 6. pii: S0195–6701(20)30046–3.
- [11] Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMc2001737>.
- [12] World Health Organization. Situation reports. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>. Accessed 22 Feb 2020.
- [13] Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from and asymptomatic contact in Germany. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMc2001468>.
- [14] C. Huang et al., “Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China,” *Lancet*, vol. 395, no. 10223, pp. 497–506, 2020.
- [15] De Groot RJ, Baker SC, Baric RS, Brown CS, Drosten C, Enjuanes L, et al. Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Announcement of the Coronavirus Study Group. *J Virol* 2013; 87: 7790- 7792.
- [16] Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. *The Lancet*. 2020; 395: 809-815.
- [17] 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. *The Lancet*. 2020; 395: 497-506.
- [18] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*. 2020; 395: 507-513.
- [19] 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. *New England Journal of Medicine*. 2020.
- [20] Backer J., Klinkenberg D., and Wallinga J., "Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travelers from Wuhan, China," *Eurosurveillance*, vol. 25, no. 5, 2020.
- [21] Natalie M.L., Tetsuro K., Yichi Y et.,al "Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of Publicly Available Case Data," *J Clin Med.*, vol. 9, no. 2, p. 538, 2020.
- [22] Unhale Subhash Shrikrushna, Ansar Bilal Quazi et.,al “A Review on Corona Virus (COVID-19)” *World Journal of Pharmaceutical and Life Science*, vol. 6, no.4, pg 109-115, 2020.
- [23] Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. *Journal of the American Medical Association* 2020. Epub ahead of print 11 March . <https://doi.org/10.1001/jama.2020.3786>
- [24] Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19).
- [25] Wu Z, Mc Googan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *Jama*. 2020.
- [26] ICMR - National Institute for Research in Reproductive Health. Guidance for Management of Pregnant Women in COVID-19 Pandemic [INTERNET] [Accessed 21 April, 2020] Available at: <http://www.nirrh.res.in/wpcontent/uploads/2020/04/Guidance-forManagement-of-Pregnant-Women-inCOVID-19-Pandemic.pdf>
- [27] Liang H, Acharya G. Novel corona virus disease (COVID-19) in pregnancy: What clinical recommendations to follow? *Acta Obstet Gynecol Scand*. 2020;99:439–442.
- [28] Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in Coronavirus Disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology*. 2020.
- [29] World Health Organization. Corona virus disease (COVID-19) Advice for the public. 2020
- [30] WHO Coronavirus disease (COVID-19) advice for the public. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public>
- [31] How to Protect Yourself, Coronavirus Disease 2019 (COVID-Coronavirus Disease 2019 (COVID-19)19), Centre for disease control and prevention. <https://www.cdc.gov/coronavirus/2019-ncov/prepare/prevention.html>
- [32] COVID-19, Occupational Safety and Health Administration, United State Department of labour, <https://www.osha.gov/SLTC/covid-19/controlprevention.html>.
- [33] WHO Coronavirus disease 2019 (COVID-19) Situation Report – 53, MARCH 2020 https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200313-sitrep-53-covid-19.pdf?sfvrsn=adb3f72_2
- [34] WHO Q&A on coronaviruses (COVID-19) March 2020, <https://www.who.int/news-room/q-a-detail/q-a-coronaviruses>.
- [35] World Health Organization Coronavirus Disease 2019 Situation Report. Available online: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200326-sitrep-66-covid-19.pdf?sfvrsn=9e5b8b48_2 (accessed on 25 March 2020).

- [36] Adhikari, S.P.; Meng, S.; Wu, Y.J.; Mao, Y.P.; Ye, R.X.; Wang, Q.Z.; Sun, C.; Sylvia, S.; Rozelle, S.; Raat, H.; et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: A scoping review. *Infect. Dis Poverty* 2020, 9, 29. [CrossRef]
- [37] Hopman, J.; Allegranzi, B.; Mehtar, S. Managing COVID-19 in low- and middle-income countries. *JAMA* 2020. [CrossRef]
- [38] Centers for Disease Control and Prevention 2019 Novel Coronavirus, Wuhan, China. 2020. Available online: <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html> (accessed on 13 April 2020).
- [39] World Health Organization Coronavirus Disease (COVID-19) Advice for the Public. Available online: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public> (accessed on 30 March 2020).
- [40] World Health Organization. Available online: <https://apps.who.int/iris/handle/10665/330987> (accessed on 30 March 2020).
- [41] Lippi, G.; Simundic, A.M.; Plebani, M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19). *Clin. Chem. Lab. Med.* 2020. [CrossRef] [PubMed]
- [42] Nishiura, H, "Determination of the appropriate quarantine period following smallpox exposure: an objective approach using the incubation period distribution," *Int J Hyg Environ Health*, vol. 212, no. 1, pp. 97-104, 2009.
- [43] Jin YH, Cai L, Cheng ZS, 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.
- [44] Siegel D, Hui HC, Doerffler E, et al. Discovery and Synthesis of a Phosphoramidate Prodrug of a Pyrrolo[2,1-f][triazin- amino] Adenine C-Nucleoside (GS-5734) for the Treatment of Ebola and Emerging Viruses. *Journal of medicinal chemistry.* 2017;60(5):1648-1661.
- [45] Mulangu S, Dodd LE, Davey RT, Jr., et al. A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics. *The New England journal of medicine.* 2019;381(24):2293-2303
- [46] Ng M, Lee EYP, Yang J, et al. Imaging profile of the COVID-19 infection: Radiologic findings and literature review. *Radiology: Cardiothoracic Imaging* 2020;2(1):e200034. doi: 10.1148/ryct.2020200034
- [47] Chinese Society of Radiology. Radiological diagnosis of new coronavirus infected pneumonitis: Expert recommendation from the Chinese Society of Radiology (First edition). *Chin J Radiol*, 2020,54(00): E001-E001. DOI: 10.3760/cma.j.issn.1005-1201.2020.0001.
- [48] Nishiura, H, "Determination of the appropriate quarantine period following smallpox exposure: an objective approach using the incubation period distribution," *Int J Hyg Environ Health*, vol. 212, no. 1, pp. 97-104, 2009.
- [49] Khodaei F, Ahsan A, Chamanifard M, Zamiri MJ, Ommati MM, et.al. Updated information on new coronavirus disease 2019 occurrence, drugs and prediction of a potential receptor. *Journal of biochemical and molecular toxicology.* 2020; 34, issue 8.