



COVID-19 : An Overview

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Abstract: COVID-19 an infectious respiratory illness caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), has now spread to multiple countries including INDIA. The outbreak of corona virus disease-2019 (COVID-19) caused by SARS-CoV-2 has threatened health worldwide. There have been about approximately 96000 reported cases of corona virus disease 2019 and 3300 reported death to date (05/03/2020). The disease infected by the contact with infected droplets and the incubation period ranges from 2 to 4 days (8). Middle East Respiratory Syndrome (MERS) and COVID-19 all of these viruses are responsible for effecting acute respiratory tract infections. The RT-PCR detection of viral nucleic acid test (NTA) was one of the most suddenly organized laboratory diagnosis method in a novel viral pandemic, just as in this COVID-19 outbreak (16). The symptoms normally between 2 and 14 days after exposure. RT-PCR for SARS-CoV-2 in an Indian council of Medical Research (ICMR) appreciate medical laboratory, data regarding clinical details, exposure history, hospital causes and outcome were collected in pre-designed perform.

Keywords: SARS-CoV-2, Epidemiology, Diagnosis, symptoms, RT-PCR, treatment, drugs.

Introduction: Recently the outbreak of multitudinous infective disease has symbolically impact the lives of millions of peoples. The WHO reported that the whole number of fixed COVID-19 cases has inanced sharply to 79,231,893 (1,754,547 deaths 2.21% fatality ratio) in 219 countries/area as of December 29, 2020. The fatality ratio in France, Italy, and united kingdom reached 2.48%

(62,197 deaths 2,507,532 confirmed cases), relatively. The expand of COVID-19 is gracefully unstoppable against the world, and the global pandemic brought actual physical and physiological effect on individuals and financial loss against countries (22).

Background: In 21 December 2019, an outbreak of pneumonia of unknown origin was reported in Wuhan, Hubei section, China. Most of these cases were epidemiologically connected to the Human Seafood Wholesale Market. Indocination of bronchoalveolar lavage fluid received from patients with pneumonia of unrecognized origin into human airway epithelial cells and vero E6 and Huh7 cell line led to the isolation of a novel corona virus, SARS-CoV-2, previously named 2019-nCoV. Family of corona virus is the coronaviridae and positive single stranded RNA viruses surrounded by an envelope. Genera-Alpha, Beta, Gamma, Delta corona virus [1]. On December 31, 2019, the Chinese centre of disease control and prevention (china CDC) dispatched a quick response team to accompany Hubei provincial and Wuhan city report the results of this examination, discover the source of pneumonia clusters, and explain a novel corona virus described in patients with pneumonia whose specimens were tested by china CDC at an forward stage of the outbreak [2]. The egress of the 2019-CoV pneumonia has analogous with the 2003 outbreaks of severe acute respiratory syndrome (SARS), which was caused by another corona virus and that killed 349 of 5327 patients with confirmed infection in china [3]. On march 17, 2020, the COVID-19 outbreak was announced a national emergency in the united states as the number of cases grew over 4226 with a death toll of about. Globally, there are 105,586 infection cases reported as a march 8,2020 with 3,656 new infections while cases reported in china alone of COVID-19 pneumonia are 80,859 [4]. The pandemic of SARS-CoV-2 virus infections has caused 113,315,218 fixed cases of corona virus disease COVID-19, including 2,517,964 deaths up to 28 February 2021 in world by world health organization (WHO). The high rate of person-to-person transmission with a large number of deaths poses a suggestive threat to global public health [5]. The disease rumble to other countries, such as Thailand, Japan, Republic of Korea, Viet Nam, Germany, United State and Singapore [6]. The disease was exceedingly infectious and there was announced by the WHO as a public health emergency of International Concern (PHEIC) within a month following the first case. On march 11, WHO declared COVID-19 a pandemic disease it initiated to circulate against the globe [7].

Epidemiology: SARS-CoV-2 are enveloped positive sense RNA viruses ranging from 60nm to 140nm in diameter with spike like projection on its surface giving crown like view under the electron microscope (fig.1).

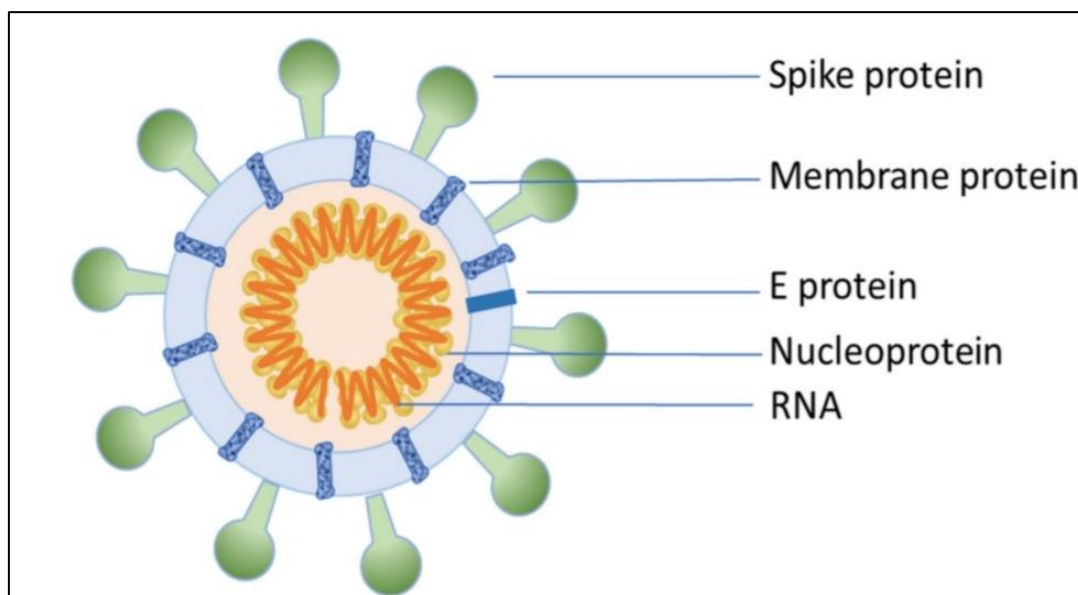


Fig. 1: Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) structure.

The first covid-19 case were intelligible in late December 2019 in Wuhan, China and the epidemic turned into a pandemic within a weeks. As of September 30, 2020 more than 33 million deaths [9]. Since SARS-CoV, MERS-CoV and SARS-CoV-2 are not well becoming to be maintained in humans, they are likely to expand mainly through other zoonotic reservoir, with unusual outbreak in the affected human population probably via an intermediate host species. especially human to human transmission rate of the novel corona virus is actually large which causes a broad spectrum of clinical explanation in patients contaminated with virus [10]. A few cases combine epidemic of the gastrointestinal tract, liver, kidney and brain. Broadcast alveolar damage epithelial cells proliferation and expansion in macrophages in seen in SARS-CoV disease of the lung. Lymphopenia, hemaphagocytosis in the lung, in extention to white-pulp atrophy of the spleen discovered in SARS patients, are identical to fatal H5N1 influenza viruses infection [11]. COVID-19 has been considered as a type self-limiting virulent disease, and most cases with benign symptoms can recover in 1-2 weeks. SARS-CoV-2 infection can causes five contrasting outcomes asymptomatic infected persons (1.2%), mild to medium cases (80.9%), severe cases (13.8%), critical case (4.7) and death (2.3% in all reported cases) [12]. All the while 2009 influenza pandemic, an access surveillence when cases become to numerous to count. This access which, can be adapted to COVID-19 associates using existing inspection systems or designing analysis to confirm each week the number of persons with a highly sensitive but nonspecific syndrome and testing subset of these persons for the novel corona virus [13].

Diagnosis: The asymptomatic performance and ease of transmission via respiratory droplets, faces and close contacts made it more crucible to authority it's wide spread transmission. Fast and correct exposure of COVID-19 is crucial to control explosion in the association and in hospitals. Current symptomatic test for corona virus include reverse transcription polymerase chain reaction (RT-PCR), real-time real time RT-PCR and reverse

transcription loop mediated isothermal amplification (RT-LAMP) [14]. The availability of the entire genome of SARS-CoV-2 previous in the epidemic promoted the evaluation of definite primers and standardized laboratory contract for COVID-19 [15]. The contract of the first real-time RT-PCR estimation targeting the RNA-development RNA polymerase (RDRP), envelop (E), and nucleocapsid (N). Genes of SARS-CoV-2 were published on 23 January 2020 [15]. The kit was chosen for it frequent and successful use in our laboratory with other estimation and it's actual opportunity primers and probes were used as characterized and provided by TIB molbiol [16]. The occupation of SARS-CoV-2 in respiratory variety identified by real-time RT-PCR enlargement of SARS-CoV-2 open reading frame lab (ORF1ab), nucleocapsid protein (NP) genes fragments using kits prepare by Shanghai Hairui Biotechnology Co. As previously characterized when two targets (ORF1ab, NP) tested positive by definite real-time RT-PCR, the case would be considered to be laboratory accepted [17]. Chest CT plays an essential role in timely distinguish lung irregularity, allowing for previous treatment. Infected patients essentially presented with fever and cough, a few patients (70%) were symptomatic [18]. As of July 15th, 2020 the number of worldwide SARS-CoV-2 active cases is all over 14 millions, with 58226 deaths and 7,881,023 recovered. current SARS-cOv-2 diagnosis test largely the ones with a EUA, have been completely reviewed some non commercial techniques that have been latterly announced in the literature are explicitly included in the report to provide the audience with the most new research based explanation and the basic outcomes [19]. Other individual from the patients can also be used for exposure of the SARS-CoV-2 RNA including bronchoalveolar lavage fluid (BLF) blood sputum, feces, urine oropharyngeal swabs and even fibro bronchoscope brush biopsies [20]. Immunochromatographic evaluation is the most commonly used method for the exposure of SARS-CoV-2 affects the human body, IgM antibody can be composed within 5-7 days is most useful for certain determining recent disease while IgG antibody can be composed within 10-15 days and may remain appreciable for months or years [21]. Analysis is based on medical and travel history, contact to COVID-19 patients and clinical disorder. Confirmation is done by exposure (RT-PCR) for nasopharyngeal swabs or bronchoalveolar fluid around 50% of nasopharyngeal swabs may be false negative.

Symptoms: The corona virus disease 2019, outbreak in Wuhan China has spread fastly with various countries. Corona virus disease caused by human to human transmission. The virus is mainly transmit by droplets, but direct contact and fecal excretion are other possible. Disorder commonly arrive between 2 and 14 days later lability. Incubation time of COVID-19 is up to 14 days. Common clinical symptoms combine fever, dry, cough, sore throat, fatigue, diarrhea, conjunctivitis, hyposmia and hypogeusia. Independent aspects for sever disease and poor outcomes are age > 65 years of life, male gender cardiovascular disorders and diabetes mellitus [22].

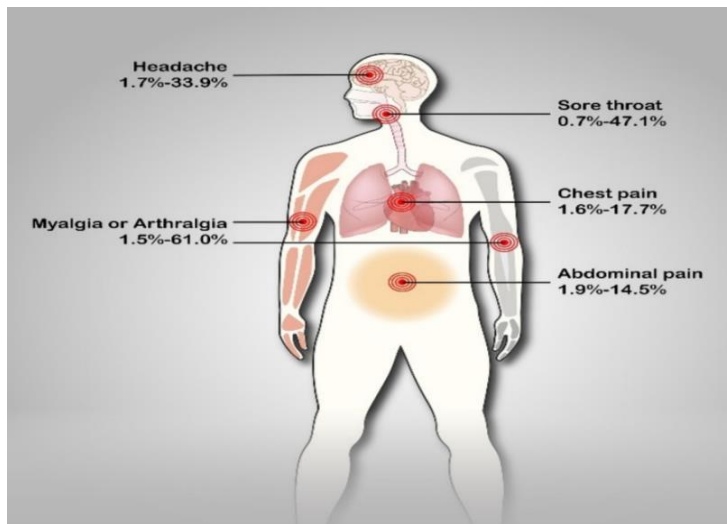


Fig. 2: Pain symptoms for COVID-19 patients.

Headache: Headache is also a actual frequent clinical symptoms and the infection with the COVID-19 is not an expulsion. When SARS-CoV-2 infect lung tissue, it may alveolar gas exchange disorder, leading to hypoxia in the brain. The main routes of COVID-19 transmission among people are close contact and droplet illness Headche is not a classical symptoms of patients with COVID-19, but it cannot clamly easily abandoned [23].

Sore throat: The throat is defined to a range of contagious and non-contagious component that cause pharyngeal, inflammation, commonly described by patients as sore throat. The NSAID Flurbiprofen has been demonstrated to be effective for the comfort of cramp of sore throat. Flurbiprofen for sore throat was advanced to observed the principle utilizing the minimum available dose of medication to achieve an excellent adequacy/safety profile [24].

CT/RT-PCR Test: March, 17 the world Health Organization (WHO) has reported over 170000 cases with over 10000 new diagnoses added in 24 hours. IN additions to being used in the clinic for contagious disease distinguishing in preceding epidemics, pooling has been accepted to work for RT-qPCR, a time-immoderate step for which the indicator are normal to be in abbreviated supply [25]. Among nucleic acid test, the polymerase chain reaction (PCR), method is consider as the “gold standard” for the disclosure of a few viruses and is characterized by accelerated disclosure immense sensitivity, and particularity As such real-time reverse transcriptase-PCR(RT-PCR) is of extreme interest for the disclosure of SSARS-CoV-2 due to it benefits as a definite and elementary approximate assessment . An essential concern with the real-time RT-PCR test is the risk of bring out false-negative and false-positive results [26]. For patients with numerous RT-PCR assessment, the aggressive alteration of RT-PCR results was concluded as correlated with serial chest CT scans for those with time-interval of 4 days more [27]. The time for

symptoms onset to improvement ranged from 12 to 32 days. Later hospital discharged or discontinuation of quarantine, the patients were ask to continue the quarantine covenant at home for 5 days. The RT-PCR tests were repeated 5-13 days later and all were positive [28]. In INDIA first laboratory-accepted case of COVID-19 was announced from Kerala on January 30, 2020. As of march 31 2020 a total of 2,245 cases and 56 deaths were reported in INDIA. assumed the severe acute respiratory illness (SARI) surveillance data (February 15 – April2, 2020) to calculate the weekly COVID-19 positivity, and characterized the circulation of COVID-19 positive SARI case by place and individuals attributes [29].

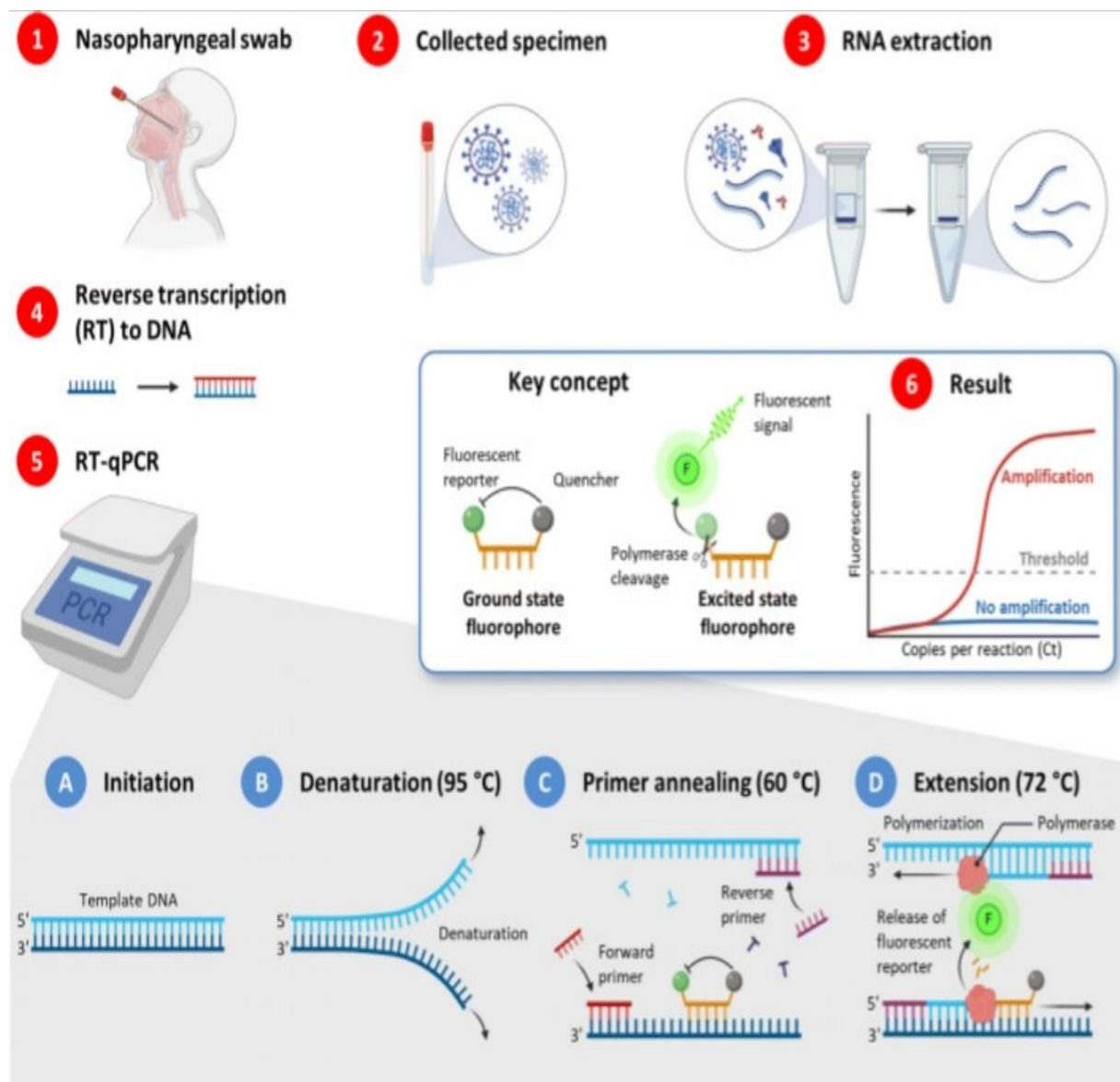


Fig. 3 A procedure of COVID-19 diagnosis through RT-PCR.

We possessed data of children younger than 12 years professed tertiary care institutes, including COVID-19 appropriated hospitals, of west Bengal [30]. RT-PCR testing can be used as an autonomous disorder tool given its big aspect for COVID-19. RT-PCR awareness in this study was approximately higher in older patients compared with

younger patients in male patients compared with female patients [31].

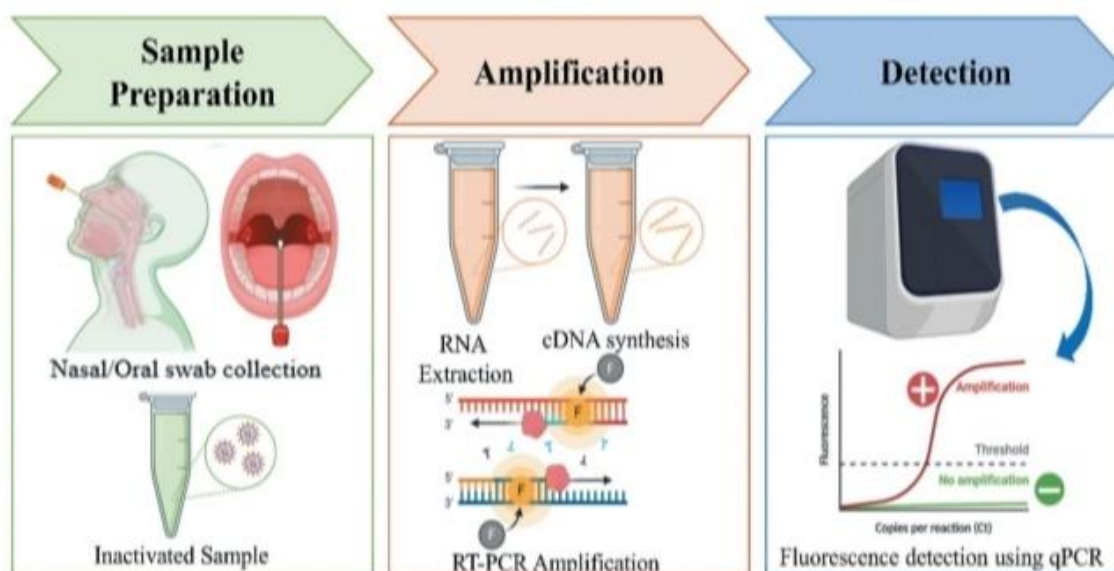


Fig. 4 COVID-19 Diagnostics Test Using RT-PCR.

According to the fig three Nasal or oral swabs are collected from infected patients containing upper and lower respiratory tract fluids. IgM antibody could be identified in patient blood after 3-4 days of SARS epidemic while IgM antibody could be purposeful 8 days of SARS disease virus [32].

Treatment: No medicine is very adequate in treating the SARS-CoV-2 infections, but the classes of drugs that are mainly used comprises antiviral agents, inflammation blockage, low molecular weight heparins plasma and hyper-immune immune-globulins [33].

Antiviral agents: The Italian medicines Agency (Agenzia Italian del Farmaco-AIFA) accepted the ARCO-home study that intention to test the adequacy of darunavir-cobicistat, lopinavir-ritonavir, favipiravir and hydroxyl-chloroquine as therapies at home in an early COVID-19 population to prevent the advancement of the disease towards genuine or critical clinical forms with the obligation to resort to hospitalization and invasive procedures such as incubation [33]. Antiviral medicines are prescription medicines that action opposite in your body.

The centre of drug evaluation and research (CDER) is matched in numerous activities to assure and benefit public health during the COVID-19 pandemic. Recently, the treatment of patients with SARS-CoV-2 virus are mainly repurposing the applicable therapeutic drugs and based on symptomatic conditions. Considering ARDS, followed by secondary infections, antibiotics antiviral therapy, systemic corticosteroids, and anti-inflammatory drugs [33].

Remdesivir: Remdesivir is a prodrug. It's active analogue arrives and assemble in cells, inhibiting viral RDRP⁴ and stopping viral replication. In animal studies, pretreatment with remdesivir conserve rhesus, monkey form MERS-CoV virus and low the severity of lung

destruction when given after lability to MERS-CoV [34]. The first case report of remdesivir help in COVID-19 begun from united states. This is a previously well 35 year old gentleman with history of hypertriglyceridemia, who was accepted for monitoring and isolation [35]. Remdesivir (45-5734) was developed by Gilead science and appear from a association between Gilead, the U.S. centers for disease control and prevention (CDC) of infectious diseases (USAMRIID) [36]. Remdesivir use was identical with a lower need for more intensive respiratory support but it did not arrive to advanced conclusion in patients who require mechanical ventilation or extra-ordinarily membrane oxygenated. Treatment was given for 5 days as correlated with 10 days [37]. Remdesivir is a narrow molecule monophosphoramidate prodrug. It is and adenosine analogue that blocks the RNA dependent RNA polymerase through it's nucleoside component. Competing with ATP, RDV-TP incorporate (ATP) by RDRP and viral RNA chain complex leading incomplete termination of viral RNA transcription and subsequent RNA synthesis inhibition [38].

Chloroquine and Hydroxychloroquine: To desirable benefit of chloroquine, a largely used anti-malarial drugs, in treatment of patients infected by the novel emerged coronavirus (SARS-CoV-2). The sulfate and phosphate salt of chloroquine have both been degrade as ant-malarial drugs. The only moderated effect of chloroquine in the therapy of human virus disease was established for chronic hepatitis C an increase of the initial virological response to pegylated interferon [39]. Chloroquine is not FDA accepted for analysis of COVID-19 On June 15 2020 the FDA revoked the EUA for chloroquine stating that it is improbable to be adequate in treating COVID-19 [40]. Hydroxychloroquine and chloroquine possibly do not reduce mortality or mechanical ventilation and may not reduce period of hospitalization. The evidence does not eliminate the potential for a narrow increased risk of death and mechanical ventilation with hydroxychloroquine [41]. Chloroquine is used to prevent and treat malaria and amebiasis, while hydroxychloroquine (HCQ) a less noxious metabolite of chloroquine is used to treat rheumatic disease such as systemic lopus erythematosus (SLE), rheumatoid arthritis (RA). While commonly considered secure several adverse effects of HCQ and CQ have been announced gastrointestinal discomfort being the most common [42].

Favipiravir: Favipiravir an oral, broad spectrum RDRP inhibitor an already accepted drug for new and reemerging pandemic. Favipiravir-RTP binds to and RNA dependent RNA polymerase (RDRP), which basically prevents viral transcription and replication oral [43]. Favipiravir was accepted for treatment of novel influenza on February 15, 2020 in Chaina. It is transformed by host enzymes to T-705-ribofuranosyl 5'- triphosphate and possible acts as a nucleotide analog that selectively inhibits the viral RNA dependent RNA polymerase or causes lethal mutagenesis upon embodiment into the virus RNA without cytotoxicity to mammalian [44].

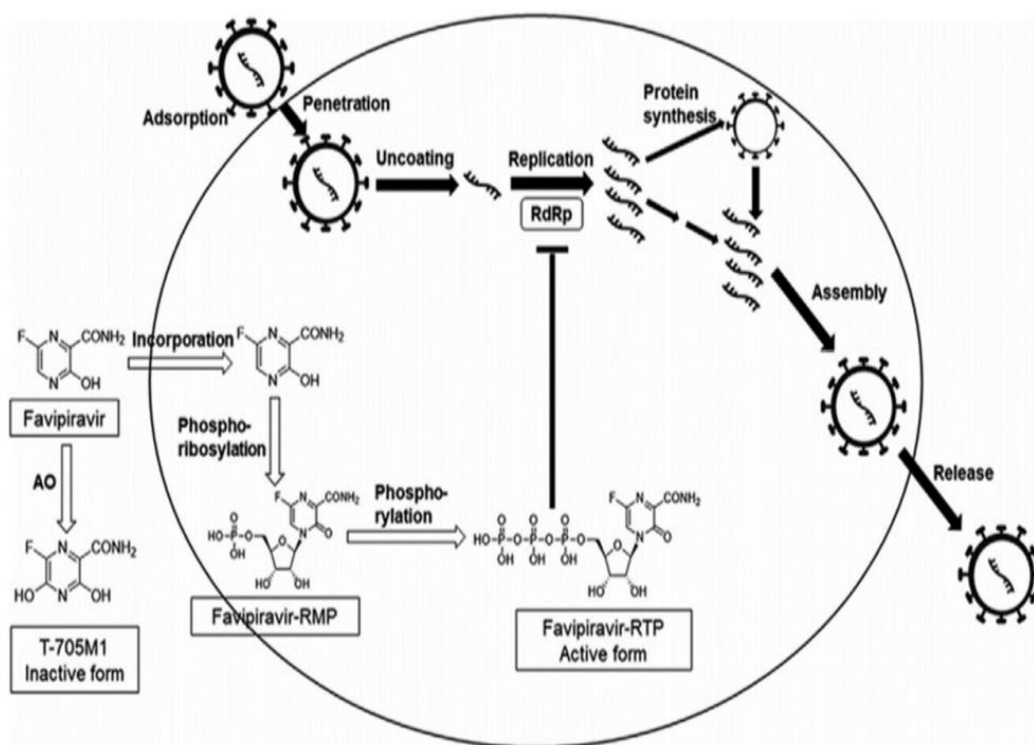


Fig.5 Favipiravir MOA in SARS-CoV-2.

Favipiravir was developed by the Fujifilm toyama chemical company and it licenced in Japan and China. In 2014, favipiravir was accepted in Japan for use in the event of an outbreak of novel or remarking influenza viral infectuion. The drug is found to be well tolerated for healthy voluntears it is contraindicated for use in pregnancy because of teratogenic and embryotoxic effects noted in animals [45]. Favipiravir it has been used for treatment of a few life threatening infection such as Embola, Lassa, Fever, and Rabies and its therapeutic usefulness. A positive effect of favipiravir was also recommended in a case series by Doi et al, who used a combination of favipiravir and nafamostat mesylate, which display promising results in seriously ill COVID-19 patients. Favipiravir is a promising drug treatment of COVID-19 that might contraction the hospital stay and the need mechanical ventilation [46].

Lpoinavir/Retinovir: It is a protease inhibitor and nucleoside analog combination used for human immunodeficiency virus (HIV-1) and was also thought to be a capacity treatment for COVID-19 was assessed by in-vitro studies that claimed inhibition of several viral corona respiratory illness, and including severe acute respiratory syndrome (SARS-COV-2),and middle east respiratory syndrome (MERS-CoV) only recently, LPV/RTV therapy was hypothesized to be of no antiviral ability opposite SARS-CoV or MERS-CoV [47]. The primary outcome was 28 days all cause fatality, the trial is registered with 1SRCTN, 50189673. The drug concert lopinavir-ritonavir has been recommended as an antiviral treatment for COVID-19 [48].

Nelfinavir: Nelfinavir mesylate was advanced as anti-human immunodeficiency virus (HIV) protease inhibitor. Also it was announced that nelfinavir mesylate inhibited SARS replication and cytopathic effect in cell culture. In addition to its potent action opposite the HIV protease nelfinavir mesylate was found to produced various on cellular processes including the induction of cell defensive mechanism including cell cycle [49]. Nelfinavir to 30 capability target proteins of COVID-19, we found that nelfinavir is most apparently a multi-target agent. Nelfinavir was appreciable in bronchoalveolar lavage fluid in 100% patients treated in 4 weeks. The concentration of nelfinavir in the lung epithelial lining fluid was begin to be analogous to the concentration begin in plasma, showing the high penetration potential of nelfinavir into the alveolar compartment [50]. Nelfinavir mesylate was bought from R and D systems, Inc (MN) and dimethyl sulfoxide (DMSO) was concentrated from sigma, Inc (St Louis, MO) [51].

Baricitnib : Baricitnib is a small molecule capricious Janus-associated kinase (JAK) inhibitor authorized in over 65 countries for the treatment of adults with moderate to severe rheumatoid arthritis (RA). Baricitnib has the asset of providing in vitro antiviral action at concentration accomplished with approve dosing [52]. In hospitalized patients with COVID-19, baricitnib was identical with reduced 28 days fatality although there was not a statistically compelling reduction in advancement [53]. Baricitnib may also have antiviral activity. It's potentiality antiviral activity was consistent by searching large riposte of structured medical and dry information echoed using maching learning (Benevolent , London, UK)[52].

Azithromycin: Azithromycin presents in vitro activity against SARS-CoV-2 and could act in distinct points of the vigorous cycle. Azithromycin has been recommended as a power analysis for the treatment of SARS-CoV-2 pneumonia given it's antiviral and immunomodulatory activity with a acclaimed secure profile [54]. It has been shows that Azithromycin has compelling antiviral properties. Azithromycin is authorized in both adults and children aged > 6 months. First approved in the USA in 1991, it has been directed to numerous patients and it's resistance is well known [56]. Azithromycin could act on SARS-CoV-2 adhesive to respiratory cell. It's intracellular aggregation led to an boost in the PH that may impair trans-Golgi network (TGN) and lysosome action [54]. The most constant adverse drug reaction are related to gastrointestinal tract [56]. Azithromycin is an acid stable orally administered macrolide antimicrobial drug. Azithromycin is lightly less active than erythromycin in vitro against Gram-positive organisms [57]. Azithromycin could act on SARS-coV-2 binding to respiratory cells. The expansion of the lysosomal PH by Azithromycin may also alter the indocytosis action and lysosomal proteases activity, which may ambitious the synthesis process [58].

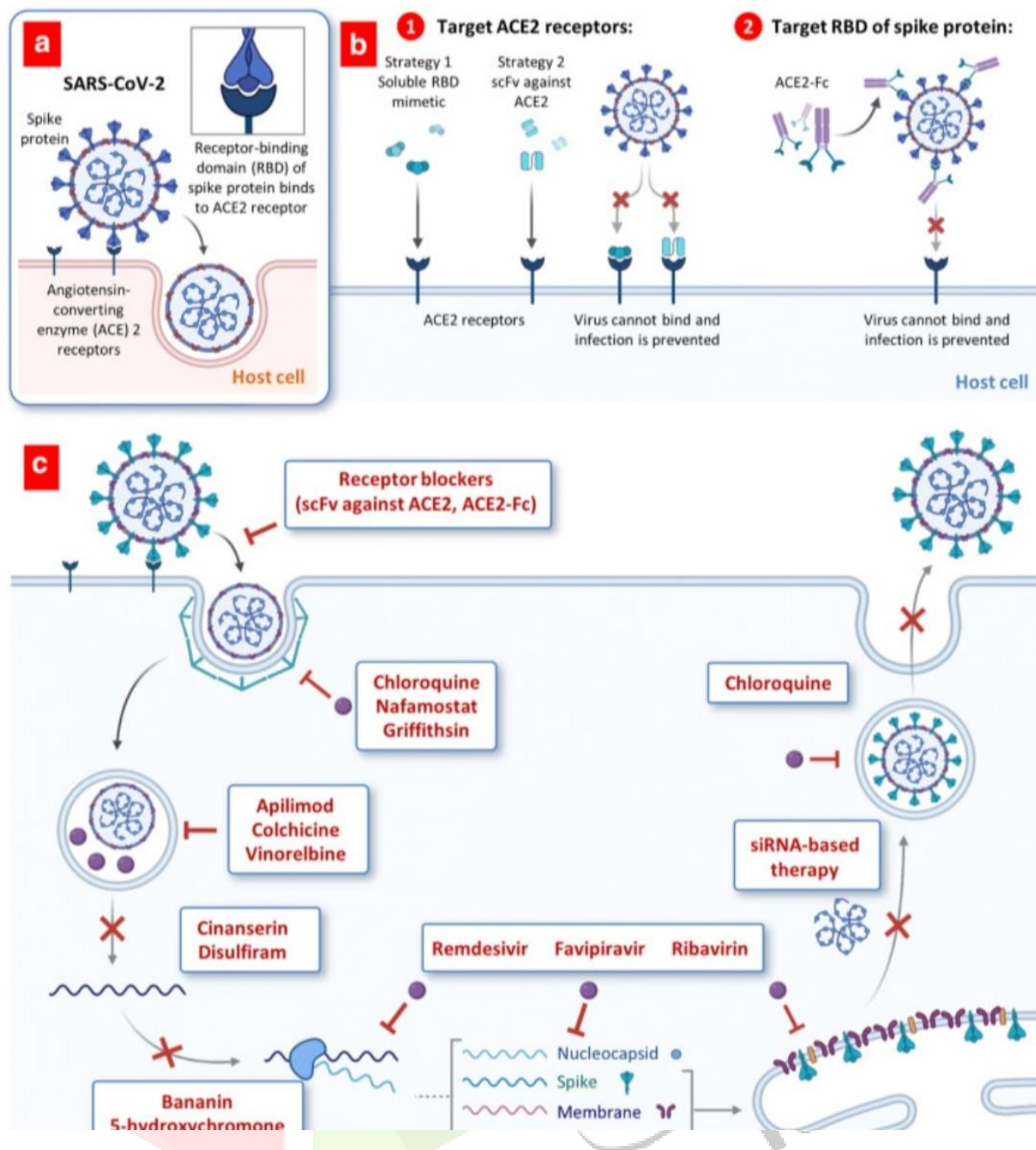


Fig. 6 Therapeutic treatments for COVID-19.

Mutation of SARS-CoV-2 virus: The highest well-known mechanism of mutation is the random genetic drift, which plays a role in the processes of transcription, translation, replication, etc. however, the host gene alteration has been begin to be the major source for existing SARS-CoV-2 mutations, counting for 65% of reported mutation [57]. Even if the D614G mutation is established in the virus external spike protein that receives a lot of attention from the human immune system . The D614G mutation is unlikely to have a major impact on the potency of vaccines currently in the RBD [58]. As a fundamental biological process, mutagenesis changes the organism genetic information and sever as a primary source for many kinds of cancer and heritable diseases, which is a driving force for evolution [59].

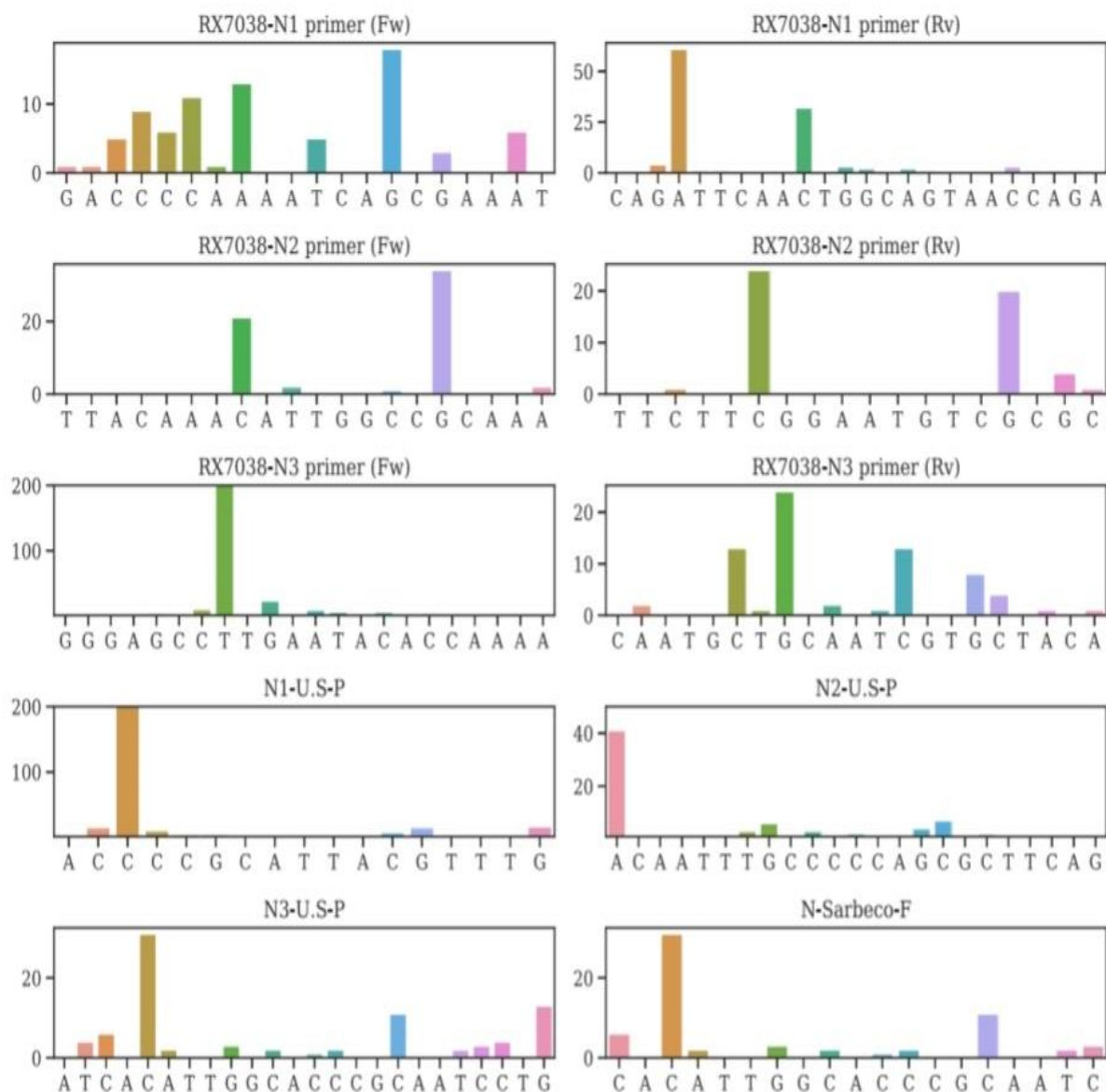


Fig . 6 : Mutation positions and frequencies one of the primer/or probes of RX7038-N1 primer (Fw), RZ7038-N1 primer (Rv), RX7038-N2 primer (Fw), RX7038-N2primer (Rv), RX7038-N3 PRIMER (Fw), RX7038-N3 PRIMER (Rv), N1-U.S.-P, N2-U.S.P, N-Sarbeco-F.

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