An Elsevier Indexed Journal ISSN-2230-7346

Journal of Global Trends in Pharmaceutical Sciences

REVIEW ON COVID-19: A GLOBAL PANDEMIC DISEASE

Milind J. Umekar[1]*, Karandeep Kaur R. Rai[1],Rashmi V. Trivedi[1], Nishant A. Dokarimare[2], Mayur B. Kale[2]

[1,1*,2]Smt. Kishoritai Bhoyar College of Pharmacy, New Kamptee, Nagpur, Maharashtra-441002 (India)

*Corresponding author E-mail: drmilindumekar@gmail.com

ARTICLE INFO

Key Words

Coronavirus, transmission, pathogenesis, drug therapies

Access this article online Website: https://www.jgtps.com/ Quick Response Code:

ABSTRACT

Coronavirus disease (COVID-19) is caused by severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) signifies the causative agent of a potentially lethal disease that is of abundant world-wide public health concern. It was emerged in Wuhan, China and spread globally. On 30 January 2020, World Health Organization (WHO) officially professed the COVID-19 epidemic as a public health emergency of international concern. In accordance to the genomic analysis, Genomic analysis revealed that SARSCoV-2 is phylogenetically related to severe acute respiratory syndrome-like (SARS-like) bat viruses, therefore bats could be the possible primary reservoir. Despite of unknown intermediate source, the rapid human to human transfer has been widely assured.Extensive strategies have come forward to reduce person-to-person transmission of COVID-19 in order to control the current outbreak. Special attention and efforts should be taken into consideration to protect or reduce transmission in susceptible population including children, health care providers, and elderly people.There is no clinically approved antiviral drug or vaccine available till date against COVID-19. However, investigations have been carried out using broad-spectrum antiviral drugs against COVID-19 in clinical trials,that resulted in clinical recovery. In this review, we have discussed about the symptoms,structure, epidemiology, transmission, pathogenesis, diagnosis and potential treatment availability to control the spread of this fatal disease.

INTRODUCTION

A cluster of pneumonia with unknown aetiology came into existence in late December 2019 had unfold Wuhan city , China and to different countries across the globe [1-2]. The initial spread in the patients was epidemiologically linked to a wet sea food market. Subsequent isolation of virus from infected personnel and further analysis at molecular level revealed the pathogen as a novel coronavirus 2019 was named as COVID-2019 by WHO (World Health Organization) on 11 February, 2020. In accordanceto the group of International Committee on Taxonomy of Viruses (ICTV) recommended the name SARS-CoV-2. The novel coronavirus seemed to be member of Coronaviridae family known to infect humans. With the immense number of increase in confirmed cases, WHO declared the outbreak as a public Health Emergency of International Concern (PHEIC) on 30th January 2020 [3]. Under microscopic examination, structure of virus appeared to be of crown –like and in latin , word corona means " crown". Phylogenetic information implicatea zoonotic o rigin, and also the speedy spread suggests in progress person to-person transmission. Transmission of coronaviruses from contaminated dry surfaces has been postulated together with self-inoculation

of mucous membranes of the nose, eyes or mouth [4,5] , accenting the importance of a close understanding of coronavirus persistence on inanimate surfaces [6]. Person-to-person spread of COVID -19 seems to occur principally by respiratory transmission, however simply the virus is transmitted between persons is presently unclear. Signs and symptoms of COVID-19 embody fever, cough, and shortness of breath [7] . Based on the incubation period of malady for middle east respiratory syndrome (MERS) and severe acute respiratory syndrome(SARS)coronavirus es, furthermore as empirical information from reports of travel-related COVID-19, Centre for Disease Control and Prevention estimates that symptoms of COVID-19 occur within 2- 14 days after exposure. Preliminary information recommends that older adults and persons with underlying health conditions or compromised immune systems could be at bigger risk for severe illness from this virus [8] .The number of cases have been reported by many countries that include Taiwan, Thailand,Vietnam, Malaysia, Nepal, Sri Lanka, Cambodia, Japan, Singapore, Republic of Korea, United Arab Emirates, United States, The Philippines, India, Australia, Canada, Finland, France, and Germany.In this review, we will discuss about the symptoms, structure, epidemiology, transmission, pathogenesis, diagnosis and potential treatment availability till date to control the spread of this fatal disease.

ADVICE FOR THE GENERAL PUBLIC: WHO/Europe continues to encourage people to take care of their own health and protect others by:

• Washing hands with water and soap or using hand-sanitizing gel;
• Maintaining social distancing by keeping a three feet distance between yourself and anyone who is coughing or sneezing:
• Avoid touching eyes, nose and mouth;
• Following respiratory hygiene (covering your mouth and nose along with your bent elbow or tissue when you cough or sneeze, then casting off the used tissue immediately);
• Seeking medical aid early if you've got a fever, cough and difficulty breathing; and
•Staying conversant and following recommendation given by your health-care provider, national and native public health authority, or your employer on a way to protect yourself and others from COVID-19.

SYMPTOMS: The COVID-19 virus affects totally different individuals in several ways. It is a disease and mostly infected people tends to develop mild to moderate symptoms.Peoplethat have underlying medical conditions and those over sixty years old have a higher risk of developing severe malady and death. Common symptoms include fever, tiredness, dry cough. Other symptoms include shortness of breath, aches and pains, sore throat and very few people can report diarrhoea, nausea or a runny nose [9,10].

STRUCTURE OF CORONAVIRUS:

Coronaviruses belong to the family Coronaviridae in the order Nidovirales [12-13]. They can be classified into four genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus **(Figure 4a**). Among them, alpha and betacoronaviruses infect mammals, gamma coronaviruses infect avian species, and delta coronaviruses infect each mammalian and avian species. Coronaviruses are large, enveloped, positive–stranded RNA viruses. They need the largest genome among all all ribonucleic acid viruses, usually ranging from twenty-seven to thirty-two kilobyte.

The genome is packed inside a helical capsid shaped by the nucleocapsid protein (N) and an encircled by an envelope. Related to the viral envelope are atleast three structural proteins: The membrane protein (M) and the envelope protein (E) are concerned in virus assembly, whereas the spike protein (S) mediates virus entry into host cells. Some coronaviruses conjointly encrypt an envelope-associated hemagglutin-esterase protein (HE). Among these structural proteins, the spike forms large protrusions from the virus surface, giving coronaviruses the appearance of having crowns (hence their name; corona in Latin suggests that crown (**Figure 4b**). in addition to mediating virus entry, the spike is a vital determinant of viral host range and tissue tropism and a major inducer of host immune responses. It was reported that the

sequence of genome of SARS-CoV-2 is 96.2 % identical to a bat CoVRaTG13, however it seemed to share about 79.5% similarity to SARS-CoV. Based on the genome sequencing results, bat has been found to be a host of transmission and via unknown intermediate hosts to infect humans. It is evident in utilising ACE-2 receptor to infect people. In genus of alphacoronavirus , it represent human coronavirus NL63 (HCoV-NL63), porcine transmissible gastroenteritis coronavirus (TGEV), porcine epidemic diarrhea cronavirus (PEDV), and porcine respiratory coronavirus (PRCV); severe acute respiratory syndrome coronavirus (SARS-CoV), Mideast respiratory syndrome coronavirus (MERS-CoV), bat coronavirus HKU4, mouse hepatitis coronavirus (MHV), bovine coronavirus (BCoV), and human coronavirus OC43 within the genus Betacoronavirus; avian infectious bronchitis coronavirus (IBV) and porcine deltacoronavirus (PdCV) within the genus Gammacoronavirus and Deltacoronavirus respectively. (b) General structure of prefusion coronavirus spikes, showing the receptor-binding subunit S1, the membrane-fusion subunit S2, the transmembrane anchor (TM), the intracellular tail (IC), and also the viral envelope. (c) Schematic illustration of the domain structure of coronavirus spikes, comprisingthe S1 N-terminal domain (S1-NTD), the S1 C-terminal domain (S1-CTD), the fusion peptide (FP), and heptad repeat regions N and C (HR-N and HR-C). Scissors designate two proteolysis sites in coronavirus spikes. (d) Outline of the structures and functions of coronavirus spikes. The S1 domains are angiotensin converting enzyme 2 (ACE2), aminopeptidase N (APN), dipeptidyl peptidase 4(DPP4), carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1), and sugar [13].

EPIDEMIOLOGY:

In December 2019, several pneumonia cases that were clustered in Wuhan town were rumoured and searches for the source have shown Human seafood market as the origin. The primary case of the COVID-19 epidemic was discovered with unexplained pneumonia on Gregorian calendar month 12,2019 and 27 viral pneumonia cases with seven being severe, were formerly proclaimed on December 31, 2019 [14,15]. Etiologic investigations have been performed in patients UN agency applied to the hospital because of similar viral medical histories of those patients has strengthened the probability of an infection transmitted from animals to humans[16, 17] .On January 22, 2020, novel CoV has been declared to be originated from wild bats and belonged to group 2 of beta-coronavirus that contains Severe Acute respiratory Syndrome Associated Coronavirus (SARS-CoV). Although COVID-19 and SARS-CoV belong to the same beta coronavirus subgroup, similarity at genome level is merely 70th, and the novel cluster has been found to indicate genetic variations from SARS-CoV [18]. Similar tothe severe acute respiratory syndrome epidemic,this outbreak has occurred throughout the Spring festival in China, which is the most noted traditional festival in China, during that nearly 3 billion individuals travel co untrywide. These conditions caused favorable conditions for the transmission of this highly contagious disease and severe difficulties in prevention and management of the epidemic. The duration of the spring carnival of China was in between Jan 17 and Feb 23 in 2003, the SARS epidemic peaked, whereas the period of the carnival was between Jan 10 and Feb 18 in 2020. Similarly, there was a rapid increase in COVID-19 cases between Jan 10-22. Wuhan, the center of the epidemic with ten million population, is additionally a crucial center in the spring pageant transportation network. The calculable number of travellers throughout the 2020 spring festival has risen 1.7 folds compared with the number travelled in 2003 and reached to 3.11 billion from 1.82 billion. This large-scale travel traffic has conjointly created favorable conditions for the unfold of this difficult-to-control malady [19]

SURVELLIANCE REPORT OF COVID -19 IN EUROPEAN COUNTRIES:

http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/weekly-surveillance-report[20]

- The number of cases reportable within the European Region doubled compared to Epidemiological week (Epi week)13/2020
- 67% of the cases were stated from Italy, Spain, Germany and France
- 75% of the deaths were reported from Spain, Italy, and France
- Nine countries and territories reported a accumulative incidence >200/100,000 population
- One out of 13 reportable infections with dataobtainable was in a health care employee
- 95% of deaths were in persons aged 60 years and older and 68% of all deaths were in males
- 91% of deaths with information accessible had a minimum of one underlying condition
- There was a steep increase in the pooled excess all-cause mortality in 24 countries and regions primarily in the age bracket >65 years, but conjointly in the 15-64 years age group for week 14/2020 (see European Mortality Bulletin)
- In Epi week 14/2020, the proportion of COVID-19 detections in persons with influenza-like malady in the primary care setting was 1 chronicles (3 countries) compared to 6% in Epi week 13/2020 (6 countries)

The corfirmed cases of COVID -19 are reported in 213 countries reached to 16,14951 in which 99887 are the confirmed death cases.

VIROLOGY-PATHOGENESIS:

The genome structure of coronavirus is well known among all RNA viruses. Two-thirds of RNA encoded viral polymerase (RdRp), RNA synthesis materials, and two large non-structural polyproteins are not associated in host response modulation (ORF1a-ORF1b). However, one-third of the genome encodes four structural proteins (spike (S), envelope (E), membrane (M) ve nucleocapsid(N), and the other helper proteins.Even though the length of the CoV genome has shown high variability forORF1a/ORF1b and four structural proteins, it is mostly linked with the number and size of accessory proteins [21,22]. The primary step in virus infection being the interaction of sensitive human cells with Spike Protein. Further leads to the genome encoding after entering to the cell helps in facilitating the expression of the genes that ultimately encodes useful accessory proteins, which leads to the adaptation of CoVs to their human host[22]. The changes in genome changes as an outcome from recombination, gene exchange, gene insertion, or deletion are frequent amongCoVs, and this will take place in future outbreaks as in past epidemics. As a result of the studies, the CoV subfamily is rapidly expanding with new generation with a sequence of applications that improve the detection and characterization of novel CoV species. In nutshell, the classification of CoV is continually changing. According to the most recent classification of The International Committee on Taxonomy of Viruses (ICTV), there are four genera of thirty-eight unique species [22]. SARS-CoV and MERS-CoV that attach to the host cell respectively bind to cellular receptor angiotensin-converting enzyme 2 (SARS-CoV associated) and cellular receptor of dipeptidyl peptidase 4 (MERS-CoV associated) [23]. After getting entered to the cell, the viral RNA manifest itself in the cytoplasm.The encapsulation and polyadenylation of genomic RNA occurred and encodes various structural and non-structural polypeptide genes. These polyproteins splits by proteases that exhibit chymotrypsin-like activity [22,23]. The resulting complex drives (-) RNA production through both replication and transcription. The full-length (-) RNA copies of the genome are produced and used as a template forfull-length (+) RNA genomes during replication [21, 22]. Asubset of 7-9 sub-genomic RNAs, comprising those encodingall structural proteins, are produced by discontinuous transcription.Viral nucleocapsids are combined from genomicRNA and R protein in the cytoplasm and then are buddedinto the lumen of the endoplasmic reticulum. Virions arethen released from the infected cell via exocytosis.The released viruses can infect kidney cells, liver cells, intestines,and T lymphocytes, as well as the lower respiratorytract, where they form the main signs and symptoms [23]. Remarkably, the count of CDT lymphocyte was found to be lowerthan 200 cells/mm3 in three patients with SARS-CoV infection. In-vitro studies revealed that, MERS-CoV is able to affect human dendritic cells andmacrophages. T- lymphocytes seems to be a target forthe pathogen due to the characteristic CD26 rosettes. By stimulating T-cell apoptosis, this virus can make the antiviral T-cell response irregular, thus causing a

collapseof the immune system[24, 25]. The virus-host interactions affected by viral entry and replication. SARS-CoV-2, being an enveloped positivesingle-stranded Ribonucleic acid (ssRNA) coronavirus. The encryption of 16 non-structural proteins (NSPs) done by common fractions of viral RNA, chiefly found in the initial open reading frame (ORF 1a/b). The one third part of the virus genome encodes four essential structural proteins, including spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein, and conjointly several accessory proteins. S glycoprotein of SARS-CoV-2 binds to host cell receptors, angiotensin-converting enzyme 2 (ACE2), that is a vital step for virus entry.Other virus proteins alsosupport pathologic process.Moreover, host factors influence susceptibility to infection and illness progression. The susceptible population involving the elderly (> 65 years of age) and people with certain underlying medical conditions, needs additional attention and care. RBD, receptor-binding domain; HR1, heptad repeats 1; HR2, heptad repeats 2 [24, 25]

CURRENT DIAGNOSTIC TESTS FOR COVID-19:

Laboratory diagnosis ; Specimen Collection: The US centre for disease control and prevention (CDC) recommends the collection of the upper respiratory nasopharyngeal (NP) swab. Collection of an oropharyngeal (OP) specimen has given the lowest preference, and, if collected, should be combined in the same tube as the NP swab [26]. The collected specimens of swab should be placed in a universal or viral transport medium. For the most nominal diagnosis of SARS-CoV,MERS-CoV, and SARS-CoV-2, it is worthwhile to collect and test both upper and lower respiratory samples i.e [sputum,bronchoalveolar lavage fluid (BAL)] [27] .Nonetheless, the collection of sputum and predominantly BAL via bronchoscopy upsurges biosafety risk to healthcare personnel through the formation of aerosol droplets. Therefore, Proper use of personal protective equipment (PPE) by healthcare workers is utmost important. Bronchoscopy is a highly technical practice will be requiring well-trained staff and it may not be offered in many parts of the world. For the patients showing mild symptoms, the specimens from the upper respiratory tract should be collected as it is easily accessible.SARS-CoV and MERS-CoV RNA can also be evidentin stool, urine and blood specimens, nevertheless less reliable than respiratory specimens collection[28-30].Apart from this, the collection from saliva specimens were tested positive in COVID -19 patients suggesting it as a promising non-invasive technique for diagnosis, monitoring, and infection control in SARS-CoV-2 infections. SARS-CoV-2 can be detected in serum, however only 15% of patients. Serum can also be the sourcefor the detection of SARS-CoV-2. However, only 15% of hospitalized patients had demonstrableRNA in serum [31]. The Specimens that has collected for laboratory testing of HCoVs should be kept at refrigerated temperature for up to 72 h, or frozen at −70°C or below. Rectal specimens have been found to be positive in patients infected with SARS-CoV-2 [32].

Cell culture: Isolation procedure of HCoVs in cell culture is not routinely performed practice for diagnosis due to the shortage of permissive cell lines, it is time consuming process, expertise requirements along with the reduced supply of antisera for culture confirmation. SARS-CoV , MERS-CoV and SARS-CoV-2 tends to grow in primary monkey cells and cell lines such as Vero and LLCMK2,but due to biosafety reasons it should not be performed in routine laboratory practices[33-36].Besides, the isolation of virus from cell cultures is criticalto acquire isolates for characterization and provision for development of vaccines and therapeutic agents.

Rapid antigen tests: Rapid antigen tests provides the theoretical advantage of rapid results and lower cost-detection of HCoVs but likely to have poor sensitivity of method used for influenza virus [37–40].Monoclonal antibodiesagainst SARS-CoV-2 have been under research. Sona Nanotech (Halifax, Canada) is emerging a quick-response lateral-flow test to screen COVID-19 patients having a target to produce results in 5–15min.The timing of specimen collection should be done when titres of virus are highest, that might improve the diagnosing sensitivity of rapid antigen tests [41].

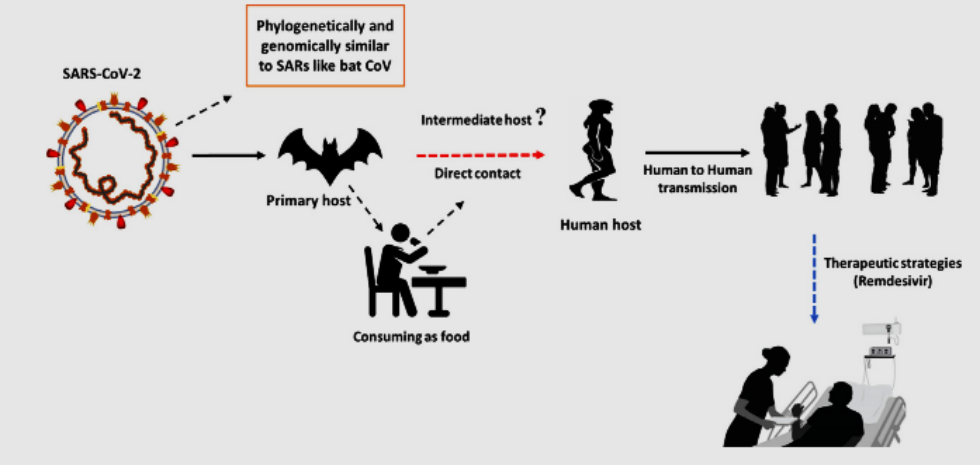

Figure 1: Mode of transmission of SARS-CoV-2[4,5]

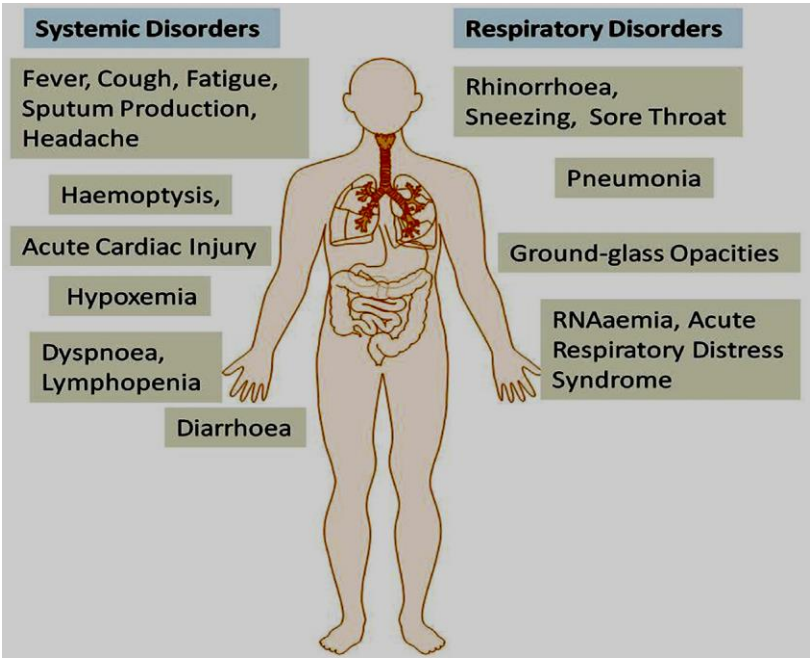

Figure 2: The systemic and respiratory symptoms caused by COVID-19 infection [11]

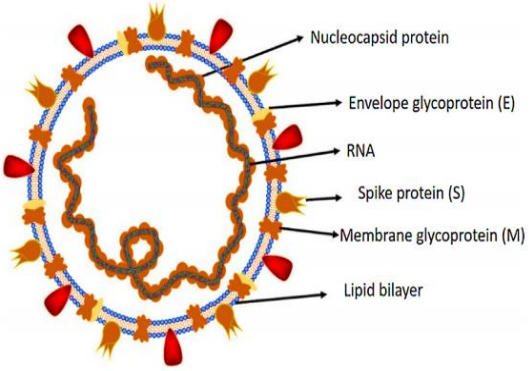

Figure 3: Structure of Coronavirus[12]

Table 1: Laboratory methods for detection of Coronavirus [33,37,41,43,55]

Method	Characteristics	Test time	Application
Antigen EIA	Rapid, poor sensitivity, some are CLIA-waived	<30 min	Diagnosis (detection)
Antigen IFA	Good sensitivity and specificity, subjective interpretation	1-4 h	Diagnosis (detection)
Cell culture	Gold standard, pure culture for further research and development, time consuming	1-7 days	Diagnosis (detection, differentiation, characterization and research)
Serology	Retrospective, cross-reaction	2-8 h	Infection confirmation, epidemiology and research, vaccine evaluation
NAAT, monoplex, pan- HCoV	High sensitivity with universal coverage of all species of HCoV	1-8 h	Diagnosis (detection), discovery and research
NAAT, monoplex, specific-HCoV	High sensitivity and specificity for special species, potential quantification	1-8 h	Diagnosis (detection, differentiation, characterization, limited typing and research)
NAAT, multiplex	High sensitivity and specificity, covering pathogens, FilmArray	1-8 h	Diagnosis (detection, differentiation, characterization, limited typing and research)
NAAT, POCT	RP EZ is CLIA-waived Rapid and safe, good sensitivity and specificity, some are CLIA-waived	15-30 min	Diagnosis (detection , limited differentiation, and research)

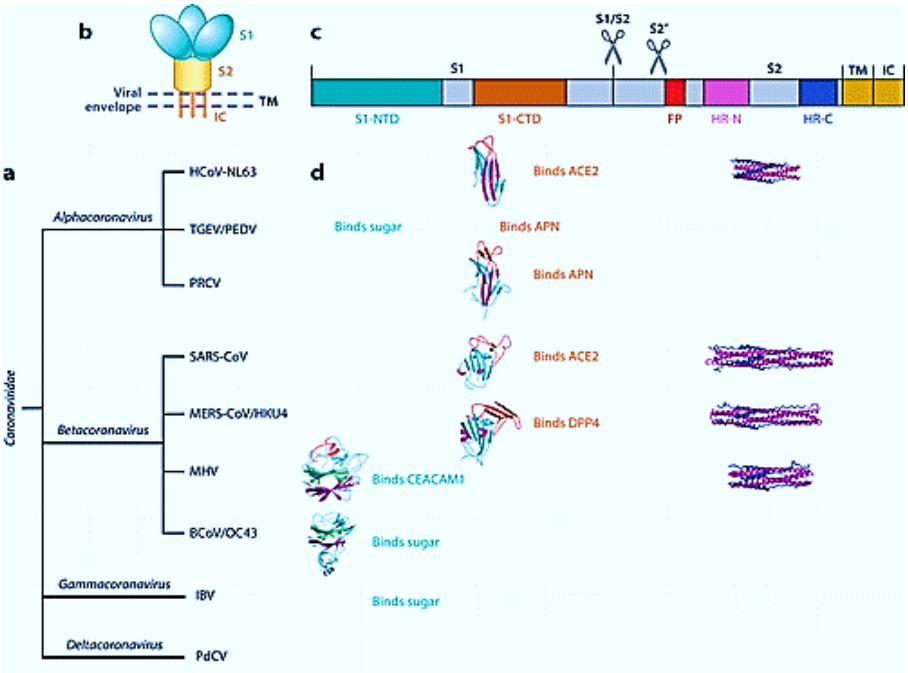

Figure 4: Introduction to coronaviruses and their spike proteins. (a) Classification of coronaviruses.

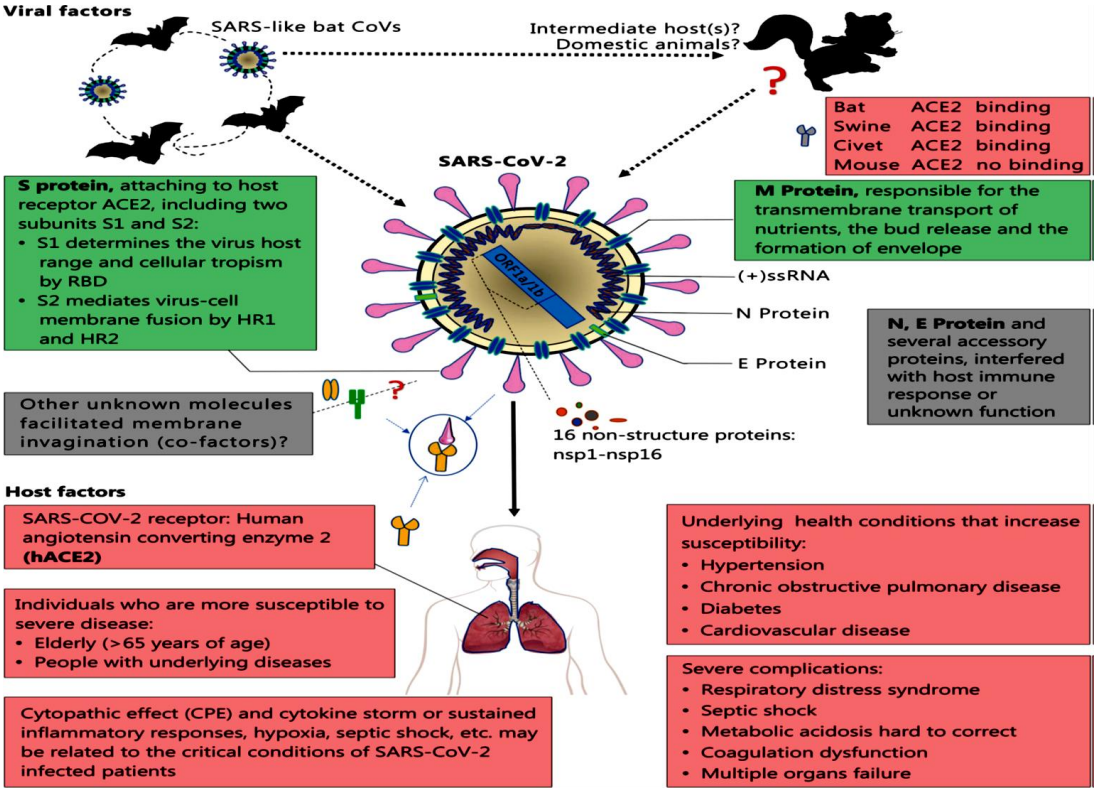

Figure 5: Viral factors originating from bats and intermediate host factors that influence the pathological process of SARS-CoV-2 and cross the species barrier into humans.

Serological assays

It has been predominantly considered method for detection of antibodies so as to analyse the novel and emergent cases ofHCoVs, such as SARS-CoV and MERS-CoV [42].It can be used as an alternative tool when molecular strategies and rapid antigen tests are neither available nor stable.A recent report revealed that both IgM and IgG antibodies were detected after five days from onset of symptoms in patients infected with SARS-CoV-2 infection.The investigations proposed to use serology tests when the collection of NP swab specimens were innapropiate and thermocellular assays were analysed unsatisfactory [43]. On 12 March 2020, urgent requirements of six serology devices got approval from National Medical Products Administration (NMPA).

Nucleic Acid Testing: It is the primary method used in the diagnosis of COVID -19 [44]. The number of kits have been designed of reverse transcriptase polymerase chain reaction (RT-PCR) in order to detect SARS – CoV-2 genetically.The process of RT-PCR incriminates the reverse transcription of SARS-CoV-2 RNA into complementary DNA (cDNA) strands, followed by amplification of specific regions of the cDNA [45,46].The design process generally comprises of two main steps: (1) Alignment of sequence and primer design, and (2) assay optimization and testing. A number of SARS- related viral genome sequences have been analysed to set a design of primers and probes. Among those SARS-related viral genomes, three regions that had conserved sequences involves : (1) the RdRP gene (RNA-dependent RNA polymerase gene) in the open reading frame ORF1ab region, (2) theenvelope protein gene(E gene),and (3) thenucleocapsid protein gene(N gene). Both the RdRP and E genes had high analytical sensitivity for detection with technical limit of 3.6 and 3.9 copies/reaction, whereas the N gene provided with a inferior analytical sensitivity of 8.3 copies/reaction. The design of assay could be a two-target system that associates with the detection of numerous coronavirus involving SARS-CoV-2, whereas set of second primers only detects SARS-CoV-2 [47].

The second step involves optimization of assay conditions, for instance incubation times, temperature and reagent conditions, to be followed by PCR testing. RT-PCR can be performed using one-step or two-step assay. In one –step assay, reverse transcription and amplification steps occurs simultaneously ad hence can provide rapid results for analysis. Its difficult to overcome the challenges of optimization and amplification steps, that ultimately leads to lower target generation of amplicon.On the other hand, two-step assay is relatively more sensitive and prepared in separate tubes, whileis time consuming requiring additional optimization parameters[48]. Upper respiratory samples including nasopharyngeal swabs, oropharyngeal swabs, nasopharyngeal washes and nasal aspirates are broadly recommended for diagnosis of COVID-19, whereas for patients exhibiting productive cough the lower respiratory tract samples comprising ofsputum, BAL fluid, and tracheal aspirates are recommended.The detectable viral load depends on the days after the onset of illness. In the paramountof 14 days SARS-CoV-2 could most reliably be detected in sputum followed by nasal swabs, converselyafter 8 days of onset of symptoms, throat swabs were unpredictable to detect[49,50].

The United States Centers for Disease Control andPrevention (CDC) practices a one-step real time RT-PCR (rRTPCR) assay, that offersquantifiable information on viral loads so as to detect the presence of SARS-CoV-2**.** In this assay, viral RNA is extracted and added to a master mix. The master mix complies of forward and reverse primers, nuclease –free water, a fluorophore-quencher probe, and a reaction mix (consisting of reverse transcriptase, polymerase, magnesium, nucleotides, and additives**)**.The next step include loading of extracted RNA and master mix into a PCR thermocycler setting the incubation temperature to run the assay. During this process, the fluorphore – quencher probe generates a fluorescent signal that is detected by the thermocycler and the process of amplification is recorded in the form of real time.CDC provides apositive control sequence called nCoVPC for SARS-Cov-2[51]**.**The workflow of RT-PCR tests includes three steps as ; first line screening , confirmation and discriminatory assays.In the first steps, all patients infected with SARS-related infections are identified by targeting different regions f E gene. If this test results positive, then the detection of RdRP were implemented by using two primers and two different probes. If these also shows positive results, then it could be followed by discriminatory tests by using one of the two probe sequences.

Computed Tomography :

Chest CT scans are known to be a non-invasive technique that involves measurements of X-ray at different angles across a patient's chest so as to get cross-sectional images.The images are further be analyzed by radiologists to find out the abnormal clinical findings which can lead to a diagnosis.Depending on the stage of infection, the diverse images of COVID-19 could be produced. The most common hallmark features of COVID-19 encompasses bilateral and peripheral ground-glass opacities (areas of hazy opacity)and consolidations of the lungs (fluid or solid material in compressible lung tissue) [52-53].

Point- of- care testing: Point-of-care tests comprises of diagnosis of patients instead of sending samples to centralized laboratories. Two approaches are generally as lateral flow antigen detection tests and microfluidic devices. In lateral flow antigen detection tests, a paper-like membrane strip is used that is coatedwith two lines: gold nanoparticle-antibody conjugates present in one line and capture antibodies in the other. The sample of patient such as blood or urine is placed on the membrane and the proteins are strained across the strip by aid of capillary action. Microfluidic devices consists of palm-sized chip imprinted with micrometer-sized channels and reaction chambers. It is usually made of polydimethyl sulphoxide, glass or paper. The chip mixes and seperates liquid samples using vacuum, electronic, and other forces. Likewise, there are many approaches that are under development such as electrochemical sensors, paper – based systems and surface – enhanced Raman – scattering systems[54-55].

Role of smartphones in diagnosis of infectious disease: Smartphones can be used in correspondence with diagnostic tests in order to

provide information that authorises not only national but also global health agencies to provide with coordinated control strategies. Several research approaches have suggested smartphones for tracking of infectious diseases such as HIV, Ebola and tuberculosis [56-57]. It can be used for contact tracing of people being infected to provide more complete and shareable records.Furthermore, it can be used to share and upload epidemiological data based on public health databases thereby coordinating the outbreak responses. It can be useful in providing communication between patients and healthcare professionals without risking lives. In 2016, Kanazawa proposed the usage of smartphones escorted by Forward Looking Infrared Radar (FLIR) for the thermal detection of body temperature caused by inflammation [58] .This type of technology may be adopted for the detection of fever, common symptom of coronaviruses includind COVID-19. A smartphone –based microscope was developed by Mudanyali that could help in addressing the point of care testing at the public level specially where the cases gone underreported [59].

COVID-19 DRUG THERAPY – POTENTIAL OPTIONS:

In general, there are few or no treatment options for viraldiseases that occur suddenly [60]. In parallel with this knowledge,today there is no vaccine or effective treatment toprevent COVID-19 infection. Studies investigating the antiviral activityof types I and II interferons have evaluated, interferon-beta(IFNb), as the most potent interferon, was able in reducing in-vitroMERS-CoV replication [61]. According to a human MERSCoVfindings reported from South Korea, provided the use of combinationtherapy of Lopinavir/Ritonavir (LPV/RTV) (Anti-HIV drugs), pegylated interferon and ribavirin for successfulclearance of virus [62].For that purpose, a randomized controltrial (MIRACLE Trial), with an aim to detect whetherLPV/RTV-IFNb improved clinical trials in MERS-CoV patients,were conducted in 2016 and 76 patients were enrolled. Although another antiviral drug, remdesivir was used inthe first case reported from the United States of America,seemed successful, controlled studies with more cases areneeded [24]. In-vitro studies have reported that Remdesivir is able to terminate viral RNA transcriptionin early stage [63,64]. There are clinical investigations demonstrating that Remdesivir hasa strong antiviral activity in epithelial cell cultures againstSARS-CoV, MERS-CoV and related zoonotic bat CoVs [65,66]. In order to avoid unnecessary panic, measures to be taken into consideration, such as timely publicationof epidemic information related to theelimination of the sourceof infection, early diagnosis, reporting, isolation and supportivetreatments . CDCreminds basic measures such as hand washing, using disinfectantsolutions, avoiding contact with patients so as to prevent the spread of viruses by droplets. Precautionaryactions including the provision of medicines supply chains,personal protective equipment, and hospital suppliesshould be made in a short time for the protection of theChinese people and global health, especially in the placeswith close travel ports to major Chinese ports [67]. Based on the 2003 SARS-CoV epidemic experience, the Chinesegovernment takes many effective measures includingclosing public transport, reduction in migration and promotingpersonal protection with masks in Wuhan and otherprovinces. Hence, the reported cases of infected hospitalpersonnel, healthcare staff should inform abouttaking personal protective measures such as the use ofgloves, eye masks and N95 masks during the examinationof patients with a suspected history of COVID-19 contact ortravel to China[68, 69].Other immunomodulating agents (e.g., alfa-interferon, sarilumab) being evaluated as adjunctive therapy [70]. On April 2, 2020 , A team at the University of Pittsburgh School of Medicine in the United States stated that - Initial clinical investigation in mice of a potential COVID-19 vaccine delivered via a fingertip-sized patch have shown to induce an immune response against the new coronavirus at the levels that might prevent infection, hoped to start testing candidate of vaccine on people in clinical trials in next few months. The vaccine tends to generate a surge of antibodies to fight against the coronavirus within two weeks. It was delivered via a fingertip-sized patch of 400 tiny needles made up of sugar and protein pieces [71]. According to the recent outbreak, antimalarial drug, hydroxychlorquine

are under investigation in clinical trials for pre-exposure or post-exposure prophylaxis of SARS-CoV-2 infection, and treatment of patients with mild, moderate, and severe COVID-19. On 28 March 2020, FDA issued an Emergency Use Authorisation (EUA) for emergency use of oral formulations of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of 2019 coronavirus disease [72].

CONCLUSION:

The outbreak of COVID-19 swept across China and spread worldwide. The extensive growth in the characterization of novel coronavirus along with the treatment approaches and vaccines have been carried out by the Research scientists across the globe. We have given a brief content about the SARS-CoV-2 as follows ; primarily the emergence of pneumonia COVID-19 caused by SARS-CoV-2. The possible modes of transmission and WHO guidelines to be followed to control the pandemic spread of disease. The clinical findings demonstrating about the systemic and respiratory symptoms. Originating from reservoir of bats and unknown intermediate hosts, SARS-CoV-2 binds to ACE2 with high affinity as a virus receptor to infect humans, the susceptible population involving the elderly and people with certain underlying medical conditions, requires more attention and care. So far, the supportingtreatments, combined with potent antiviral drugs, such as remdesivir, chloroquine, or lopinavir/ritonavir, have been conducted with definite effect to treat COVID-19 patients, while evidence from more clinical trials are in need. US scientists have developed a finger-tip sized patch that have shown to induce immune response against COVID-19 in mice that might prevent infection, the clinical trials will be carried out in next few months. The molecular mechanism of viral entry and replication may provide the basis of research on developing targeted antiviral drugs and vaccines.

Acknowledgement: The authors wish to thank Smt. Kishoritai Bhoyar College of Pharmacy for providing support and guidance for this study.

Conflicts of interest: The authors declare no conflicts of interest.

REFERENCES:

1. WHO. Coronavirus disease (COVID-19) outbreak. World Health Organization, 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019 (accessed Feb 12, 2020).
2. CDC. Locations with confirmed COVID-19 cases, global map. Centers for Disease Control and Prevention, 2020. https://www.cdc. gov/coronavirus/2019-ncov/locations-confirmed-cases.html#map (accessed Feb 12, 2020)
3. Gorbalenya, A.E. et al. (2020) Severe acute respiratory syndrome relatedcoronavirus: the species and its viruses – a statement of the Coronavirus Study Group. bioRxiv. Published online February 11, 2020. https://doi.org/10.1101/2020.02.07.93786
4. Otter JA, Donskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ. Transmission of SARS and MERS coronaviruses and influenza virus in healthcare settings: the possible role of dry surface contamination. J Hosp Infect 2016;92:235e50
5. Dowell SF, Simmerman JM, Erdman DD, Wu JS, Chaovavanich A, Javadi M, et al. Severe acute respiratory syndrome coronavirus on hospital surfaces. Clin Infect Dis 2004;39:652e7
6. Geller C, Varbanov M, Duval RE. Human coronaviruses: insights into environmental resistance and its influence on the development of new antiseptic strategies. Viruses 2012;4:3044e68
7. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507–13. https:// doi.org/10.1016/S0140-6736(20)30211-7.
8. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. China

CDC Weekly 2020. Epub February 17, 2020
9. Thompson R. Pandemic potential of 2019-nCoV. The Lancet Infectious Diseases. 2020 Mar 1;20(3):280
10. Wang W, Tang J, Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. Journal of medical virology. 2020 Apr;92(4):441-7.
11. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. Journal of autoimmunity. 2020 Feb 26:102433.
12. Enjuanes, L., Almazán, F., Sola, I. and Zuñiga, S., 2006. Biochemical aspects of coronavirus replication and virus-host interaction. *Annu. Rev. Microbiol.*, *60*, pp.211-230
13. Perlman, S. and Netland, J., 2009. Coronaviruses post-SARS: update on replication and pathogenesis. *Nature reviews microbiology*, *7*(6), pp.439-450.
14. Imperial College London. Report 2: estimating the potential total number of novel coronavirus cases in Wuhan City, China. Jan 2020. https://www.imperial.ac.uk/mrc-globalinfectiousdisease- analysis/news--wuhan-coronavirus.
15. World Helath Organization, 2019- nCoV Situation Report-22on 12 February, 2020. https://www.who.int/docs/defaultsource/coronaviruse/situation-reports/
16. Yin, Y., Wunderink, R. G.. MERS, SARS and other coronaviruses as causes of pneumonia. Respirology, 2018; 23(2): 130-137
17. Gralinski L.; Menachery V; Return of the Coronavirus: 2019-nCoV, Viruses 2020, 12(2), 135
18. Chen Z.;Zhang W.; Lu Y et. al.. From SARS-CoV to Wuhan 2019-nCoV Outbreak: Similarity of Early Epidemic and Prediction of Future Trends.: Cell Press 2020
19. Luk H. K., Li X., Fung J., Lau S. K., Woo P. C. (2019). Molecular epidemiology, evolution and phylogeny of SARS coronavirus. Infection, Genetics and Evolution. 2019; 71:21-30
20. http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/weekly-surveillance-report
21. Coronavirinae in ViralZone. Available online: https://viralzone. expasy.org/785 (accessed on 05 February 2019).
22. Lambeir, A.M.; Durinx, C.; Scharpe, S.; De Meester, I. Dipeptidyl-peptidase IV from bench to bedside: An update on structuralproperties, functions, and clinical aspects of the enzyme DPP IV. Crit. Rev. Clin. Lab. Sci. 2003, 40, 209–294.
23. Chu, H.; Zhou, J.; Wong, B.H.; Li, C.; Cheng, Z.S.; Lin, X.; Poon,V.K.; Sun, T.; Lau, C.C.; Chan, J.F.; et al. Productive replication ofMiddle East respiratory syndrome coronavirus in monocytederiveddendritic cells modulates innate immune response.Virology 2014, 454–455, 197–205.
24. Zhou, J.; Chu, H.; Li, C.; Wong, B.H.; Cheng, Z.S.; Poon, V.K.; Sun, T.; Lau, C.C.; Wong, K.K.; Chan, J.Y.; et al. Active replication of Middle East respiratory syndrome coronavirus and aberrant induction of inflammatory cytokines and chemokines in human macrophages: Implications for pathogenesis. J. Infect.Dis. 2014, 209,1331–1342.
25. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, Tan KS, Wang DY, Yan Y. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak–an update on the status. Military Medical Research. 2020 Dec;7(1):1-0.
26. Namekar M, Ellis EM, O'Connell M, Elm J, Gurary A, Park SY, Imrie A, Nerurkar VR. Evaluation of a new commercially available immunoglobulin M capture enzyme-linked immunosorbent assay for diagnosis of dengue virus infection. Journal of clinical microbiology. 2013 Sep 1;51(9):3102-6.
27. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, Spears L, Miller M, Franczyk M, Deprizio D, Schmidt GA. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. The Lancet. 2009 May 30;373(9678):1874-82

28. Al-Abdely HM, Midgley CM, Alkhamis AM, Abedi GR, Lu X, Binder AM, Alanazi KH, Tamin A, Banjar WM, Lester S, Abdalla O. Middle East respiratory syndrome coronavirus infection dynamics and antibody responses among clinically diverse patients, Saudi Arabia. Emerging Infectious Diseases. 2019 Apr;25(4):753.
29. Poissy J, Goffard A, Parmentier-Decrucq E, Favory R, Kauv M, Kipnis E, Mathieu D, Guery B, The ME. Kinetics and pattern of viral excretion in biological specimens of two MERS-CoV cases. Journal of Clinical Virology. 2014 Oct 1;61(2):275-8.
30. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; published online Jan 24.HYPERLINK"https://doi.org/10.1016/S01406736(20)301835"https://doi.org/10.1016/S01406736(20)3015(https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinicalspecimens.html.Accessed 15 March 2020)
31. Van Woensel JB, Van Aalderen WM, De Weerd W, Jansen NJ, Van Gestel JP, Markhorst DG, Van Vught AJ, Bos AP, Kimpen JL. Dexamethasone for treatment of patients mechanically ventilated for lower respiratory tract infection caused by respiratory syncytial virus. Thorax. 2003 May 1;58(5):383-7
32. Zaki AM, Van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. New England Journal of Medicine. 2012 Nov 8;367(19):1814-20.
33. Kubin CJ, Ellman TM, Phadke V, Haynes LJ, Calfee DP, Yin MT. Incidence and predictors of acute kidney injury associated with intravenous polymyxin B therapy. Journal of Infection. 2012 Jul 1;65(1):80-7.
34. Tyrrell DA, Bynoe ML. Cultivation of a novel type of common-cold virus in organ cultures. British medical journal. 1965 Jun 5;1(5448):1467.
35. Lau SK, Woo PC, Wong BH, Tsoi HW, Woo GK, Poon RW, Chan KH, Wei WI, Peiris JM, Yuen KY. Detection of severe acute respiratory syndrome (SARS) coronavirus nucleocapsid protein in SARS patients by enzyme-linked immunosorbent assay. Journal of clinical microbiology. 2004 Jul 1;42(7):2884-9.
36. Sastre P, Dijkman R, Camuñas A, Ruiz T, Jebbink MF, van der Hoek L, Vela C, Rueda P. Differentiation between human coronaviruses NL63 and 229E using a novel double-antibody sandwich enzyme-linked immunosorbent assay based on specific monoclonal antibodies. Clin. Vaccine Immunol.. 2011 Jan 1;18(1):113-8.
37. Liu IJ, Chen PJ, Yeh SH, Chiang YP, Huang LM, Chang MF, Chen SY, Yang PC, Chang SC, Wang WK, SARS Research Group of the National Taiwan University College of Medicine-National Taiwan University Hospital. Immunofluorescence assay for detection of the nucleocapsid antigen of the severe acute respiratory syndrome (SARS)-associated coronavirus in cells derived from throat wash samples of patients with SARS. Journal of clinical microbiology. 2005 May 1;43(5):2444-8.
38. Sizun J, Arbour N, Talbot PJ. Comparison of immunofluorescence with monoclonal antibodies and RT-PCR for the detection of human coronaviruses 229E and OC43 in cell culture. Journal of virological methods. 1998 Jun 1;72(2):145-52.
39. (https://sonanano.com/sona-develops-rapidscreening-test-forcoronavirus/.Accessed15 February2020).
40. Jennett B, Plum F. Persistent vegetative state after brain damage: a syndrome in search of a name. The Lancet. 1972 Apr 1;299(7753):734-7.
41. Kandeil A, Gomaa M, Shehata M, El-Taweel A, Kayed AE, Abiadh A, Jrijer J, Moatasim Y, Kutkat O, Bagato O, Mahmoud S. Middle East respiratory syndrome coronavirus infection in non-camelid domestic mammals. Emerging microbes & infections. 2019 Jan 1;8(1):103-8.
42. Yang Y, Yang M, Shen C, Wang F, Yuan J, Li J, Zhang M, Wang Z, Xing L, Wei J, Peng L. Laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infections. medRxiv. 2020 Jan 1.
43. Freeman WM, Walker SJ, Vrana KE. Quantitative RT-PCR: pitfalls and

potential. Biotechniques. 1999 Jan;26(1):112-25.
44. Kageyama T, Kojima S, Shinohara M, Uchida K, Fukushi S, Hoshino FB, Takeda N, Katayama K. Broadly reactive and highly sensitive assay for Norwalk-like viruses based on real-time quantitative reverse transcription-PCR. Journal of clinical microbiology. 2003 Apr 1;41(4):1548-57.
45. Sastre P, Dijkman R, Camuñas A, Ruiz T, Jebbink MF, van der Hoek L, Vela C, Rueda P. Differentiation between human coronaviruses NL63 and 229E using a novel double-antibody sandwich enzyme-linked immunosorbent assay based on specific monoclonal antibodies. Clin. Vaccine Immunol.2011 Jan 1;18(1):113-8.
46. Bustin SA. AZ of Quantitative PCR. San Diego. CA: International University Line [Google Scholar]. 2004.
47. Hong KH, Lee SW, Kim TS, Huh HJ, Lee J, Kim SY, Park JS, Kim GJ, Sung H, Roh KH, Kim JS. Guidelines for Laboratory Diagnosis of Coronavirus Disease 2019 (COVID-19) in Korea. Annals of laboratory medicine. 2020 Mar 31.
48. World Health Organization. Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases: interim guidance, 2 March 2020. World Health Organization; 2020.
49. Centers for Disease Control and Prevention. CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel
50. Das S, Dunbar S, Tang YW. Laboratory Diagnosis of Respiratory Tract Infections in Children–the State of the Art. Frontiers in microbiology. 2018 Oct 18;9:2478.
51. Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, Ji W. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology. 2020 Feb 19:200432.
52. Xiang J, Yan M, Li H, Liu T, Lin C, Huang S, Shen C. Evaluation of Enzyme-Linked Immunoassay and Colloidal Gold-Immunochromatographic Assay Kit for Detection of Novel Coronavirus (SARS-Cov-2) Causing an Outbreak of Pneumonia (COVID-19). medRxiv. 2020 Jan 1.
53. Foudeh AM, Didar TF, Veres T, Tabrizian M. Microfluidic designs and techniques using lab-on-a-chip devices for pathogen detection for point-of-care diagnostics. Lab on a Chip. 2012;12(18):3249-66.
54. Brangel P, Sobarzo A, Parolo C, Miller BS, Howes PD, Gelkop S, Lutwama JJ, Dye JM, McKendry RA, Lobel L, Stevens MM. A serological point-of-care test for the detection of IgG antibodies against Ebola virus in human survivors. ACS nano. 2018 Jan 23;12(1):63-73.
55. Iribarren SJ, Schnall R, Stone PW, Carballo-Diéguez A. Smartphone applications to support tuberculosis prevention and treatment: review and evaluation. JMIR mHealth and uHealth. 2016;4(2):e25.
56. Kanazawa T, Nakagami G, Goto T, Noguchi H, Oe M, Miyagaki T, Hayashi A, Sasaki S, Sanada H. Use of smartphone attached mobile thermography assessing subclinical inflammation: a pilot study. Journal of wound care. 2016 Apr 2;25(4):177-82.
57. Mudanyali O, Dimitrov S, Sikora U, Padmanabhan S, Navruz I, Ozcan A. Integrated rapid-diagnostic-test reader platform on a cellphone. Lab on a Chip. 2012;12(15):2678-86.
58. Hui D.S.; Azhar E.I:;Madani T.A.; Ntoumi F.; Kock R.; Dar O.; Ippolito G.; Mchugh T. D.;Memish Z.;Drosten C.;Zumla A.; Petersen E.; The continuing 2019-nCoV epidemic threat of novelcoronaviruses to global health -The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis, 2020 (91) ,264-266
59. Chen N., Zhou M.; Dong X.; Qu J.;Gong F.; Han Y.; Qiu Y.; Wang J.;Liu Y.;Wei Y.; Xia J.;Yu T.; Zhang X.; Zhang L.; Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020, publish onlined Jan 29, https://doi.org/10.1016/ S0140-6736(20)30211-7
60. Arabi, Y. M., Alothman, A., Balkhy et. al. Treatment of Middle East respiratory syndrome with a combination of lopinavirritonavir and interferon-β1b (MIRACLE trial): study protocol for a

randomized controlled trial. Trials 2016; 19(1); 81
61. Warren, T. K. et al. Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. Nature 531, 381–385 (2016).
62. Jordan, P. C. et al. Initiation, extension, and termination of RNA synthesis by a paramyxovirus polymerase. PLoS Pathog. 14, e1006889 (2018).
63. Cockrell, A. S. et al. A mouse model for MERS coronavirus-induced acute respiratory distress syndrome. Nat. Microbiol 2, 16226 (2016)
64. Brown, A. J. et al. Broad spectrum antiviral remdesivir inhibits human endemic and zoonotic deltacoronaviruses with a highly divergent RNA dependent RNA polymerase. Antivir. Res. 2019; 169: 104541.2019.
65. Novel Coronavirus.Prevention and Treatment. Available online: https://www.cdc.gov/coronavirus/2019-ncov/about/prevention-treatment.html (accessed on 05 February 2020)
66. Chen Z.;Zhang W.; Lu Y et. al.. From SARS-CoV to Wuhan 2019-nCoV Outbreak: Similarity of Early Epidemic and Prediction of Future Trends.: Cell Press 2020.
67. What to do if you are sick with 2019 Novel Coronavirus. Available online:https://www.cdc.gov/coronavirus/2019-ncov/about/steps-when-sick.html (accessed on 05 February 2020
68. Regeneron Pharmaceuticals. Evaluation of the efficacy and safety of sarilumab in hospitalized patients with COVID-19. Retrieved March 24, 2020. Available on the WorldWideWeb at : https://clinicaltrials.gov/ct2/show/NCT04315298?term=sarilumab&draw=3&rank=4.
69. https://in.reuters.com/article/us-health-coronavirus-vaccine-candidate/potential-covid-19-vaccine-shows-promise-in-mouse-study-idINKBN21K2BW.
70. https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html