ISBN: 978-81-946587-9-5

3. World Threat COVID-19: The Pathogenesis, Genetic Journey And Proof Based Remedial Control

Deepak Kumar Dash, Vaibhav Tripathi, Anil Kumar Sahu And Rajnikant Panik
Royal College of Pharmacy, Raipur, C.G. India.

Adeep Kujur
University Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur, C.G. India.

Abstract:

The Novel Corona virus infection (COVID 19) has become a persistent public wellbeing emergency with global impact. It is profoundly transmissible and is characterized as a pandemic of severe respiratory distress, flue like symptoms associated with brevity of breath; on the other hand asymptomatic cases have also been observed, which is become serious threat to the World. The SARS-CoV-2 viral disease started in Wuhan, Hubei Province, China in December 2019. The COVID-19 pandemic keeps developing in 216 nations/domains, around 10 021 401affirmed cases and about 499 913 confirmed deaths have been documented. In this chapter, we survey the accessible proof about the study of origin, spread dynamics, pathophysiology, examination probes and the management for COVID-19. Finding is affirmed with PCR based testing of suitable respiratory samples. A few nations are leading clinical trials to evolve and ascertain COVID-19 killing impact of existing medication and new medication moieties as well. A model medication repurposing dependent on constrained trials incorporates chloroquine, hydroxychloroquine, remdesvir, lopinavir and plasma treatment hold guarantee for the treating of COVID-19. As far as the development of vaccine is concerned genetic configuration plays significant role. New bits of knowledge into the pathophysiology, clinical highlights and management of this virus are continuously revealing by the researchers. Thus, by sharing information and extending our comprehension of the virus genetics and the illness pathogenesis, we accept that the scientific community can proficiently create viable vaccine and drugs, and the humanity will definitely win this fight against nCOVID-19 pandemic.

Keywords:

COVID-19, Asymptomatic, Pathophysiology, Virus Genetics, Drug Repurposing, Vaccine

Background:

Contagious ailments stay as the significant reasons for human and animals unhealthful and mortality, prompting huge medicinal services expenditure throughout the World, explicitly in developing nations as in India. The nation has encountered the flare-ups and epidemics of numerous infectious diseases. India, being a nation of outrageous geo-climatic decent variety, faces a steady danger of rising and reappearing viral contaminations of public wellbeing significance. At a fundamental level, rising contaminations can be characterized as those maladies whose frequency has been seen as expanded within late decades or which have taken steps to increase in future. Natural habitat demolition because of unplanned urbanization has put people at increasing contact with animals and arthropod vectors of viral diseases. Such communications have been one of the significant reasons for expanded human vulnerability to infections by novel pathogens, without distinctive immunity.

WHO reports reveal that, the source of existing and emerging infectious diseases (around 60 % and 70% respectively) in humans is zoonotic, with two-third originating in wildlife. [1]

Respiratory viral diseases, arbo-viral contaminations and bat-borne viral contaminations embody three significant classes of recent viral infections. Viral pathogens are known to cause outbreaks that have scourge and pandemic potential. At present Coronavirus (nCOVID-19) represents one of the life threatening complications in this category. [2]

Introduction:

Coronaviruses (CoVs) typically result in respiratory and enteric contaminations affecting the two creatures that is animal and people. Coronaviruses (CoVs) have a zoonotic cause from bats, aves and warm blooded creatures (most likely transmitted from bats or another host). Inadvertent research center interceded transmission may likewise be considered. [3] COVID-19 have a place with the family Coronaviridae and the order Nidovirales; [4] further separated into four genera based on protein groupings named Alpha, Beta, Gamma and Delta-coronavirus [5].

The 2019 novel CoV (SARS-CoV-2) is the most up to date expansion to human CoVs (HCoVs) that incorporate 229E, OC43, HKU1, NL63, rose in 2019 in Wuhan, China; staying two being extreme intense respiratory disorder (SARS) CoV flare-up in 2002, and Middle East respiratory condition (MERS) CoV outbreak in 2012. HCoV 229E and NL63 have a

place with Alpha-coronavirus; others are individuals in the family of Beta-coronavirus. At present these four HCoVs are tainting human populace around the world with high pace of mortality since Novel COVID-19 shows up exceptionally transmissible from human to human. [6-7]

In India, the first laboratory affirmed disease by SARS-CoV-2 was accounted for on January 30, 2020. This is the first report from India recognizing the SARS-CoV-2 infection utilizing TEM directly in a throat swab specimen affirmed by PCR.

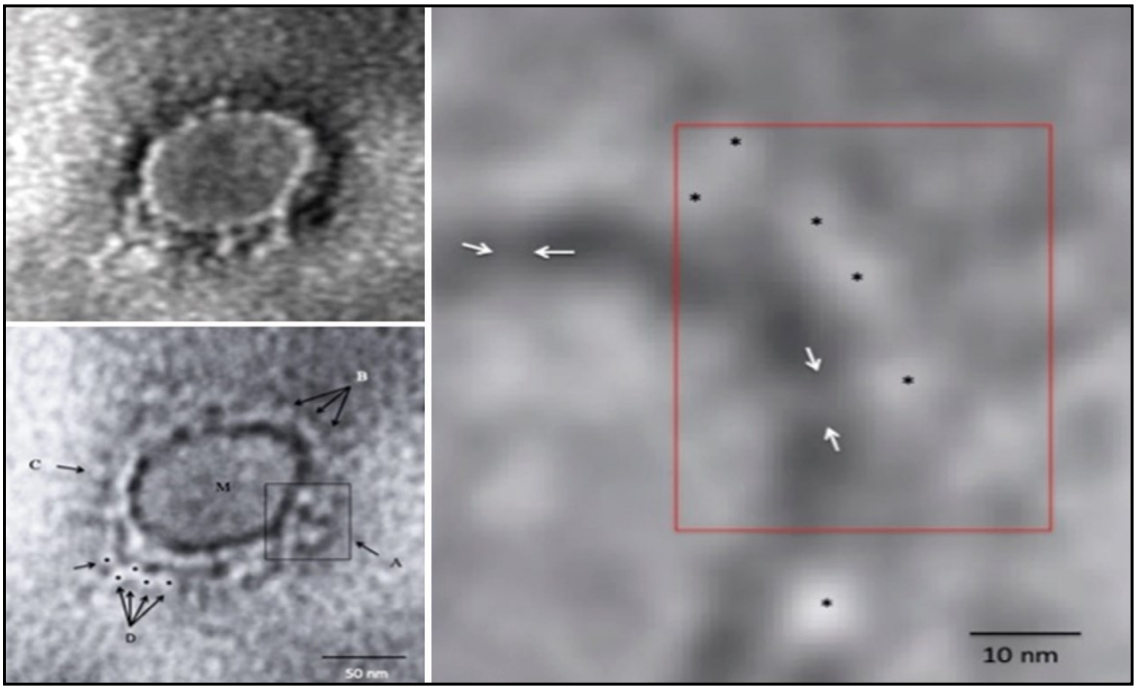

Figure 1. Transmission electron microscopy imaging of COVID-19. (A) A negative recolored COVID-19 molecule indicating morpho-demonstrative. (B) Defocussed picture of a similar molecule settling the virus envelope glycoprotein morphology in better subtleties. The boxed region A shows a tetramer-like total of four unique peplomers, bolts appeared by B show a progressively conventional morphology of coronavirus surface projections. M demonstrates the grid of the virus molecule. C shows an distinct 'peplomer head' with negative stain outline. The territory D is fascinating as conceivable direct projections could be imaged. Five particular peplomers could be imaged as appeared by the bolts. (C) A profoundly amplified handled picture for pixel amendments shows a particular proof of direct 'tail' interfacing the peplomer to the virion surface. The peplomers are appeared with bullet and the tail with a bolt. Amplification bars are incorporated with the micrographs. [8]

Genetics Configuration:

Hereditary material of HCoVs is a positive strand of RNA. The genome of COVID-19 offers about 96% replica from the bat coro-navirus BatCoV RaTG13(Rhinolophus affinis bats).[9] The extension of hereditary variety among coronaviruses and their resulting capacity to cause malady in people is mostly accomplished through tainting animals, which serve as intermediate hosts, sustaining recombination and mutation incidents. [10]

Recently, this novel CoV has been affirmed to utilize a cell passage receptor, (Angiotensin Converting Enzyme) ACE2. Its essential physiological role is in the development of angiotensin, a peptide hormone which primarily works on cardio-vascular system and controls vasoconstriction and circulatory strain. [11-13]

COVID- 19 is capable of transmitting among different host species via shifting tropism and variable receptor targeting. These characteristics are mediated by changes in the receptor binding domain (RBD) of the spike surface glycoprotein [14-15]. Their spike protein is comprised of S1 and S2 subunits, which are responsible for host receptor recognition which directly binds to the peptidase domain (PD) and membrane fusion, respectively [16- 18].

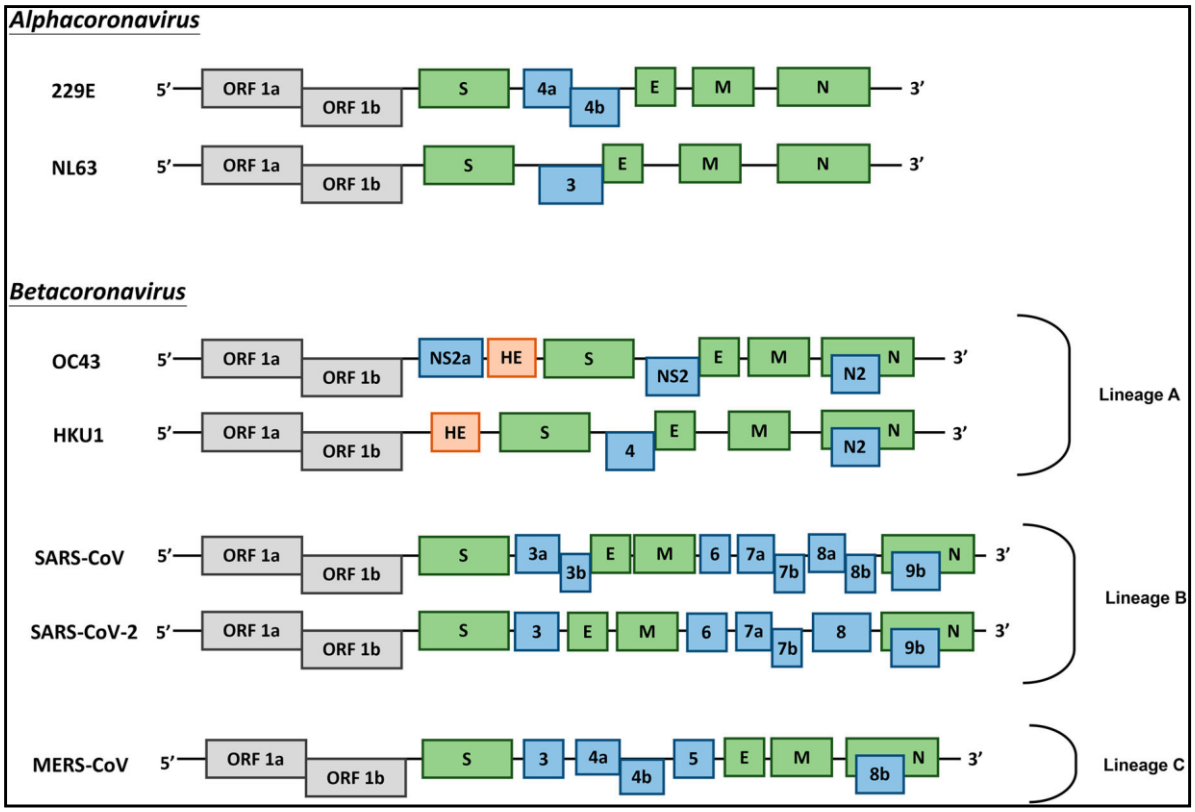

Figure 2. Genome association of HCoVs. Schematic chart of seven known HCoVs is appeared. The genes encoding basic structural proteins spike (S), envelope (E), membrane

(M), and nucleocapsid (N) are in green. The gene encoding haemagglutininesterase (HE) in lineage A of betacoronaviruses is in orange. The genes encoding embellishment proteins are in blue. [19]

Spike protein is a basic viral component that helps in the connection and infection disguise to the host cell. An immense measure of host cell receptors are focuses for viruses, including the cell surface GRP78. Hindering the communication that happens between the COVID-19 spike protein and the host cell receptor GRP78 would most likely diminish the pace of viral infection.[20]

Moreover, a vaccine for COVID-19 spike protein would probably forestall viral disease. The present in silico viewpoint proposes the presence of a COVID-19 spike protein-GRP78 restricting site, therefore establishing the road map for drug designers to create reasonable inhibitors to prevent the binding and henceforth the disease. Future work including the elements of GRP78 and the exploratory approval is required to propose intense peptidomimetic inhibitors. [21]

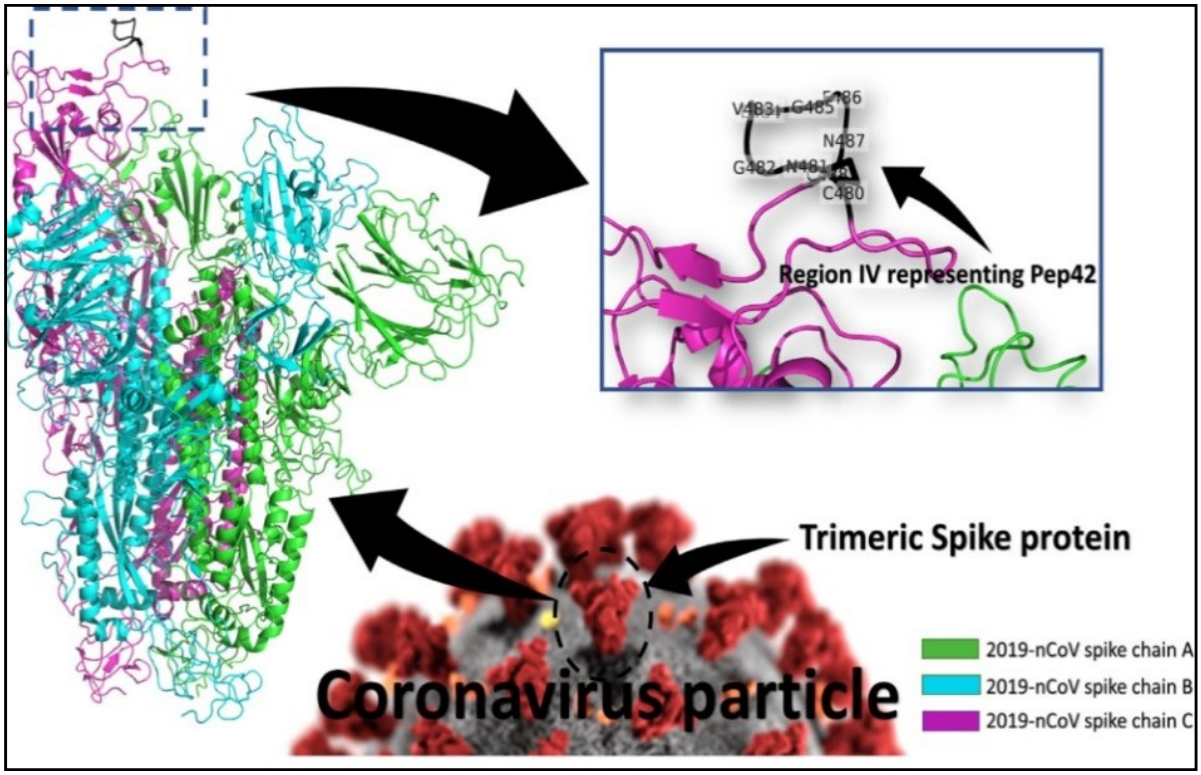

Figure 3. The structure of the spike protein model of COVID-19 in its homo-trimmer state (hued animation). Two chains, A (green) and B (cyan) are in the shut compliance, while chain C (fuchsia) is the open setup that makes it ready to perceive the host cell receptor.

Locale IV of the spike (C4 80-C4 88), which is proposed as the acknowledgment site for cell-surface GRP78, is appeared in the black animation in the extended board. [22]

In India, initial three instances of SARS-CoV-2 with a movement history from Wuhan, China, were indicated practically complete (29,851 nucleotides) genomes of case 1, case 3 and a divided genome for case 2 were gotten. The successions of Indian SARS-CoV-2 however not indistinguishable indicated high (~99.98%) character with Wuhan seafood market pneumonia infection (accession number: NC 045512). Indian SARS-CoV-2 groupings demonstrated two changes 408 Arg→Ile and 930 Ala→Val in the spike protein contrasted with the Wuhan Hu-1 succession. The changes were additionally mapped on the spike protein model of the Indian sequence. Omission of a three-nucleotide stretch, encoding tyrosine buildup at position 144, of the spike gene was likewise seen in the Indian SARS-CoV-2 from case 1 when contrasted with the remaining SARS-CoV-2 sequences.

Phylogenetic investigation indicated that the Indian successions had a place with various groups. Anticipated straight B-cell epitopes were seen as amassed in the S1 space of spike protein, and a conformational epitope was recognized in the receptor-restricting area. The anticipated T-cell epitopes indicated wide human leucocyte antigen allele inclusion of A and B super sorts overwhelming in the Indian populace [23].

Phylogenetic varieties have likewise been seen in COVID positive patients, who had originated from Italy, Iran and other European nations. RT-PCR conclusion has affirmed some division of changes to one another in the genome of the patients coming from various nations. [24]

Source And Spread:

A few current examinations based on meta-genomic sequencing have proposed that a gathering of jeopardized little warm blooded creature known as pangolins (Manis javanica) could likewise harbor tribal beta-CoVs identified with SARS-CoV-2 [25]. However, as of now there is no proof on the side of an immediate pangolin root of SARS-CoV-2 because of the succession uniqueness between SARS-CoV-2 and pangolin SARS-CoV-2-related beta-CoVs. The transformative pathway of SARS-CoV-2 is bat based on hereditary qualities. [26-27]

It has been accounted for that a bat CoV named ARCoV.2 (Appalachian Ridge CoV) identified in North American tricolored bat showed cozy relationship with HCoV-NL63 [28]. Then again, HCoV-229E was hereditarily identified with another bat CoV, named Hipposideros/GhanaKwam/19/2008, which was recognized in Ghana [29], while camelids have additionally been suspected as its middle host [30-31]. For clearness, the present information on creature roots of known HCoVs is summed up in Figure 4.

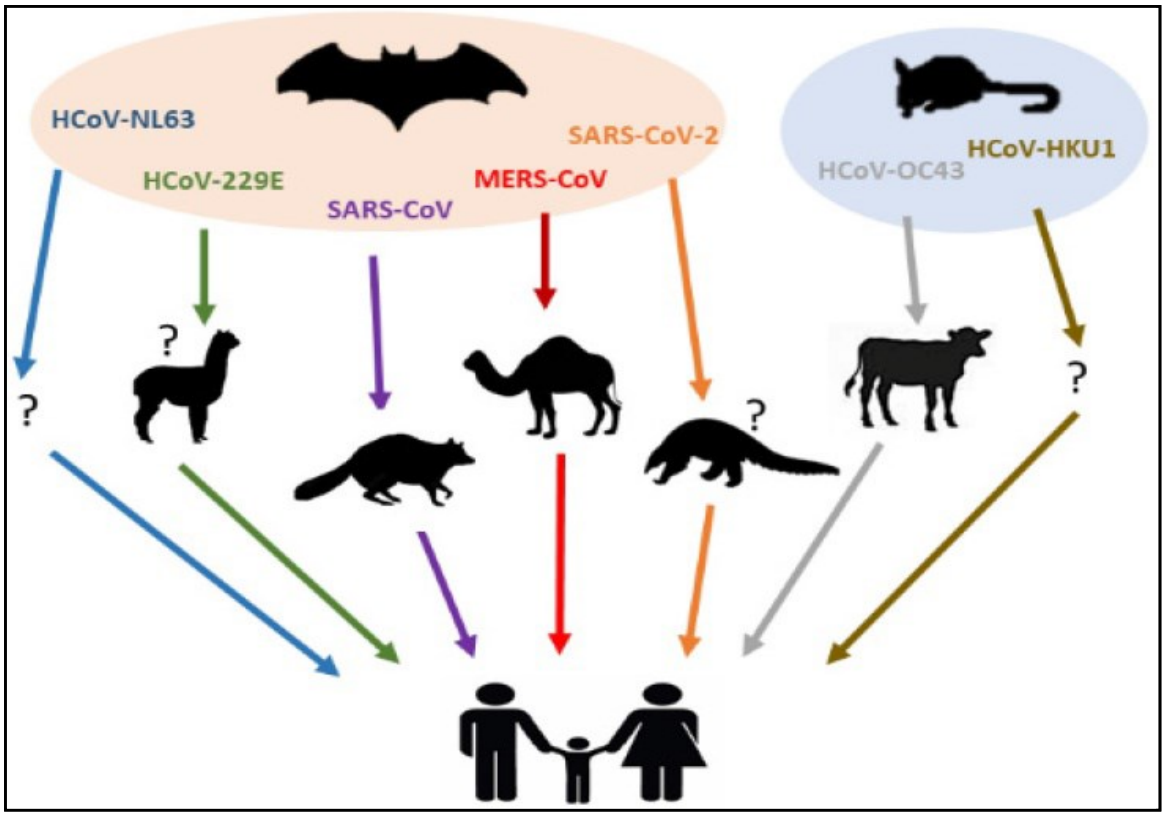

Figure 4. Creature hosts of HCoVs. Blue, green, purple, red, orange, dim, earthy colored bolts depict the transmission of HCoV-NL63, HCoV-229E, SARS-CoV, MERS-CoV, SARS-CoV-2, HCoV-OC43 and HCoV-HKU1 from their characteristic hosts (bats or rodents) to the middle hosts (camelids, civets, dromedary camels, pangolins or bovines), and in the end to the human populace. No solid proof exists on the intermediated host(s) of HCoV-NL63 and HCoV-HKU1, which was appeared as a question mark (?).[32]

The decent variety of bat CoVs gives plentiful chances to the rise of COVID-19. In this sense, bat CoVs serve as the genetic supply of SARS CoV-2. Furthermore, fast transformation and hereditary recombination likewise drive nCOVID-19 advancement and fill in as two significant strides in this process.[33-35] For instance, the obtaining or loss of

novel protein coding qualities can possibly radically change viral phenotypes. Among SARS-CoV embellishment proteins, ORF8 has been believed to be significant in adjustment to people, as SARS-CoV-2 related bat infections were disconnected however found to encode dissimilar ORF8 proteins. [36-37]

Last but not least, the development of novel COVID-19 is additionally determined by the choice in their repository hosts. Asymptomatic or just gentle manifestations were identified when bats were tainted with CoVs, showing the shared adjustment among CoVs and bats [38-39]. It created the impression that bats are all around adapted to CoVs anatomically and physiologically. For instance, defects in the initiation of pro-inflammatory reaction in bats proficiently lessen the pathology activated by COVID [40]. Furthermore, the characteristic executioner cell action in bats is stifled due to up regulation of inhibitory natural executioner cell receptor NKG2/CD94 and low articulation level of significant histocompatibility complex class I atoms [41-42].

Recent, COVID-19 disease may be begun from the contact among people and civets in the market (China), shutting wet markets and executing civets in that could have successfully finished the SARS scourge. By the same reasoning, pangolins ought to be expelled from wet markets to forestall zoonotic transmission, taking into account the revelation of numerous heredities of pangolin beta-CoVs firmly identified with SARS-CoV-2. In any case, regardless of whether and how SARS-CoV-2 is transmitted to people through pangolins and different well evolved creatures stay to be explained in future examinations. [43]

The way of life of eating wild creatures in certain spots of China should be deserted to diminish superfluous contact among people and creatures. Albeit bats have numerous highlights that favor the spreading of infection, the possibility for people to be in contact with bats and other untamed life species can be limited if individuals are taught to avoid them. With the trials of SARS, MERS and COVID-19, a superior readiness and reaction plan should be set up. [44-46]

An asymptomatic bearer of SARS-CoV-2 was accounted for in the first investigation of a family cluster [47]. Transmission of SARS-CoV-2 from an asymptomatic transporter to close contacts was later recommended, yet this has hence been tested. Notwithstanding, regardless of whether relatives and close contacts could be contaminated by the index patient in the pre-indicative window period as claimed, it is as yet deserving of a huge concern. Assumed

transmission of SARS-CoV-2 from an asymptomatic carrier to relatives has recently been recorded [48].

Second, the transmission of SARS-CoV-2 from asymptomatic carriers and pre-symptomatic patients could be even rare, if their viral burdens are low and infection shedding is not significant and for those with no upper respiratory clinical issue [49].

Hypothetically, asymptomatic transporters may emerge when have antiviral safeguard is either solid or decoupled. At the point when the immune response effectively confines however could not totally hinder SARS-CoV-2 replication, asymptomatic shedding may happen. [50]

SARS-CoV-2, the operator of COVID-19, basically spreads by beads from mucous layers (eyes, nose, and mouth), is effectively transmissible (reproduction number R0: 2–3, which means one contaminated individual, could taint three), and can spread through asymptomatic or insignificantly symptomatic people [51]. SARS-CoV-2 fundamentally spreads by coughing, sniffling, droplet inward breath, and physical contact. SARS-CoV-2 has been identified in salivation tests, making spit a potential transmission course for COVID-19 [52]. It has a middle hatching time of five-to-six days and a time of infectivity stretching out from two days before indication beginning to about fourteen days after ailment beginning in extreme cases. [53-54]

Symptoms:

SARS-CoV-2 has hereditary features vary fundamentally from those of serious intense respiratory condition coronavirus (SARSCoV) and Middle East respiratory disorder coronavirus. It is principle clinical introductions are fever and respiratory manifestations. Notwithstanding, a few patients may likewise give neurologic signs, for example, cerebral pain, queasiness, and regurgitating or loss of smell, taste and even encephalitis. [55]

The SARS-Cov-2 first overwhelmingly contaminates lower aviation routes and ties to ACE2 on alveolar epithelial cells. COVID-19 is intense inducers of inflammatory cytokines. The "cytokine tempest" or "cytokine cascade" is the proposed mechanism for organ harm. The virus enacts immune cells and instigates the discharge of fiery cytokines and chemo-kines into pulmonary vascular endothelial cells. The primary clinical signs of COVID-19 are fever

(90% or more), cough (around 75%), and dyspnea (up to half). A little yet noteworthy subset has gastrointestinal manifestations. [56-57]

Laboratory assessment shows that absolute quantity of leukocytes, neutrophils and lymphocytes decline in many patients, while CRP increases significantly and pro-calcitonin is typically normal. The principle signs on CT are inconsistent/punctate ground glass opacities with a solitary flap or various projections involvement. [58]

Susceptibility To Covid- 19:

The danger of death from COVID 19 seems to be in those matured greater than 40 years and presumably connected to other severe medical history, specifically prior medical problems including heart ailment, respiratory scatters, diabetes, cancer and dementia. [59]

Besides, a few authors detailing early perceptions from China, seem to recommend that a potential cytokine storm or fulminant myocarditis might be pre-determinants of danger of death from this sickness; with raised heart troponin, myoglobin, C-receptive protein and Interleukin-6 being indicators of danger of death. As the proof advances, are these markers which we ought to be routinely be surveying in affirmed cases of COVID 19. [60]

Likewise it is by all accounts that information are developing that kids are probably going to give milder indications than older adults, with an ongoing research recommending that 13% of youngsters who screen positive are asymptomatic, 42% have mellow upper respiratory tract symptoms, 45% exhibit regular (adult) manifestations, and no kid has extreme or critical highlights. [61]

Diagnosis:

The disease rate is considerably thought little on the grounds that a noteworthy extent of COVID-19 patients have not been affirmed by polymerase chain reaction (PCR), due to the fact numerous patients, particularly more youthful ones, have just scarcely any symptoms if any, and numerous patients with manifestations are not tested. It has been estimated that the absolute number of COVID-contaminated individuals is around five times higher than the official measurements. This inclination must be considered when deciphering any COVID-19 statistics. [62]

In a study, synthetic or artificial intelligence (AI) using a 3 dimensional profound gaining knowledge of model is reported tremendously touchy and particular for the prognosis of COVID-19. This model is structured on proof based totally and realistic measures to compliment, and include an amalgamation of the modern-day technological advances on rising approaches to enhance control and especially determination of this rising pandemic (Figure 5). [63-64]

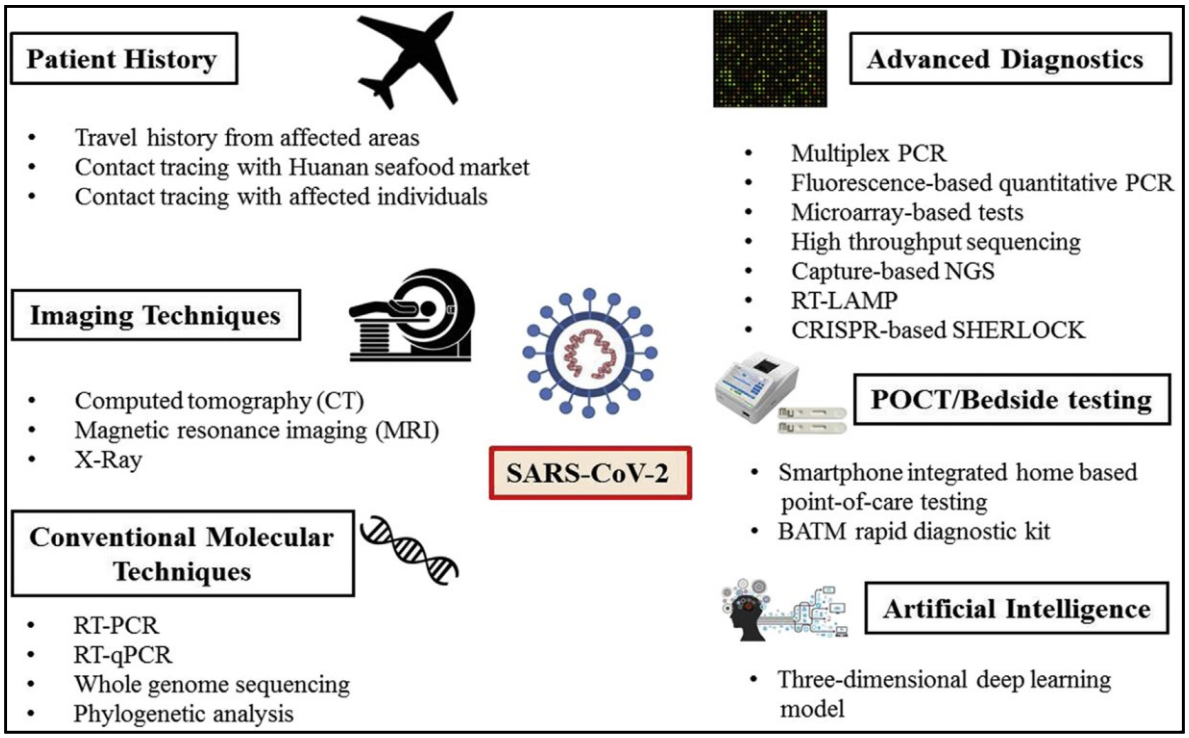

Figure 5. Significant check-points identified with the current innovative advances on developing ways to deal with improve control and especially diagnosis of the SARS-CoV-2/COVID-19 pandemic NGS (Next Generating Sequencing); RT-LAMP (Reverse Transcriptional Loop-Mediated Isothermal Amplification); CRISPR-based SHERLOCK (Specific High Sensitivity Enzymatic Reporter UnLOCKing); POCT (Point-Of-Care Testing)

There are barely any accessible methodologies that can recognize SARSCoV-2, from the standard research facility tests to the quick symptomatic tests with incredible application capacity to help decreasing the labor of recurring laboratory test.

Antibody Based Protein Level Detection: This test is led with patient's serum to check if the patients have the precise counter acting antibody against SARS-CoV-2's antigen. Since

this technique is certifiably not an immediate identification of SARS-CoV-2 infection, there can be a vulnerable side when the samples are detected as negative.[65-66]

Nucleic Acid Amplification Tests (NAAT): The significant research assay to affirm whether patients are tainted with SARSCoV-2 or not is through the nucleic acid amplification tests (NAAT), for example the real-time reverse transcription polymerase chain reaction (rRT-PCR). To painstakingly affirm the disease, three areas of the SARS-CoV-2 RNA successions are chosen for the measure: coding area for spike protein, ORF1, and ORF8. [67-69]

Numerous molecular demonstrative probes have been allowed by Emergency Use Authorization (EUA) and Food and Drug Administration (FDA) to recognize SARS-CoV-2 positive patients. Three significant molecular probes are as followed: -

The Xpert SARS-Cov-2 Xpress Assay: It is a sub-atomic in vitro indicative test using broadly practiced real time RT-PCR intensification tool to identify the nucleo-capsid quality (N2) and the envelope quality (E) in upper respiratory samples. [70-71]

The ID NOW COVID 19 Assay: It is a fast atomic in vitro analytic test using isothermal nucleic acid amplification technology to recognize the RNA-dependent RNA polymerase (RdRp) gene fragment of the SARS-CoV-2 virus. [72]

The Eplex Assay: It is an in vitro diagnostic test that objectives the N gene of SARS-CoV-2 and utilizations combined electro wetting technology for the extraction, intensification and identification with the help of competitive DNA hybridization and electrochemical probes. [73]

In a clinical assessment, it was found that the Xpert Xpress had the most reduced constraint of detection that is highly sensitive (100% recognition at 100 copies/mL), accompanied by using the ePlex (100% detection at 1,000 copies/mL), and the ID NOW (20,000 copies/mL). The Xpert Xpress likewise had most elevated positive percent agreement (PPA) when contrasted with the reference standard (98.3%) alongwith ePlex (91.4%) and ID now (87.7%). [74]

Clusters of Regularly Inter-Spaced Short Palindromic Repeats (CRISPR) Technique: Meanwhile, researchers around the globe are constantly searching and exploring innovative

strategies for the identification of SARS-CoV-2. For instance; a dynamic gene altering probe CRISPR method has been applied to effectively distinguish manufactured SARS-CoV-2 RNA successions. [75-76]. More recently, a completely novel approach that combines a unique RNA amplification (reverse transcription enzymatic recombinase amplification, RT-ERA) and a fluorescence resonance energy transfer (FRET)-based probe has proposed. [77]

In India, three continuous RT-PCR assays are practiced [based on the RNA dependent RNA polymerase (RdRp) gene, envelope (E) gene and nucleo-capsid (N) gene], which are best for spotting COVID-19 with the aid of in vitro transcribed (IVT) RNA for SARS-CoV-2; targeting E gene, while the corroborative RdRp test utilized purged RNA of SARS-coronavirus Frankfurt 1 strain as positive control . [78]

Clinical Management:

There are no precise treatments endorsed by the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC) for extreme intense respiratory syndrome coronavirus SARS-CoV-2, the infection that causes coronavirus malady 2019 that is COVID-19. A few agents are being utilized under clinical trial and strict protocol dependent regimen to validate in vitro activity against SARS-CoV-2 on confined medical experience. Till now, viability has not been built up for any medication therapy. [79]

Comprehension of the treatment of sufferers with COVID-19 is hastily evolving. Drug regimen data will keep on developing with respect to pharmacologic treatment for SARS-CoV-2 as new clinical information will get approval.

A list of currently used medicines is followed:

S. No.	Drug	Class	Mode of Action	Safety Concern	References
01	Chloroquine	Anti-Malerial	Inhibition of viral enzymes; ACE2 cellular receptor inhibition	Risk of cardiac-arrhythmias; Caution in patients with G6PD deficiency, Caution in diabetics	80-82
02	Hydroxy chloroquine	Anti-Malerial	Same as Chloroquine	Same as Chloroquine	83-86

S. No.	Drug	Class	Mode of Action	Safety Concern	References
03	Lopinavir; Retonavir	HIV Protease Inhibitor	Replication enzyme (M^{Pro}) inhibitor	Risk of cardiac arrhythmias; Caution in patients with hepatic disease or hepatitis	87-90
04	Remdesivir	Anti-Viral	RNA dependent RNA- polymerase inhibitor	Contraindicated in pregnancy according to animal study	91-95
05	Favipiravir	Anti-Viral	RNA dependent RNA- polymerase inhibitor	Contraindicated in pregnancy according to animal study	96-99

Table 1. List of medicines

Supportive Therapy:

S. No.	Drug	Class	Mode of Action	References
01	Azithromycin	Macrolide	Immunomodulator Cytokine IL- 8 inhibitor	100-102
02	Siltuximab	Monoclonal Antibody	Interleukin IL-6 receptor-inhibitor	103-105
03	Leronlimab	Monoclonal Antibody	Immunomodulator Cytokine release syndrome	106-108
04	COVID-19 Convalescent Plasma	Plasma Antibody	Immunomodulator	109-112

Table 2. List of supportive medicines

The main stay of all information about COVID-19 is to develop effective treatment. Recently, angiotensin-converting enzyme 2 (ACE2) has been demonstrated to be a utilitarian receptor for SARS-CoV-2 to enter target cells. It is observed that angiotensin receptor blockers (ARBs) and an ACE inhibitor (ACEI) up directed ACE2 articulation in animal examines, the worry may emerge with respect to whether ARBs and ACEIs would build the grimness and mortality of COVID-19. Then again, animal data proposed a potential defensive impact of ARBs against COVID-19 pneumonia in light of the fact that an ARB forestalled the exacerbation of intense lung injury in mice tainted with SARS-CoV-2, which is firmly

identified with SARS-CoV-2. Critically, in any case, there is no clinical or test proof supporting that, ARBs and ACEIs either enlarge the weakness to SARS-CoV-2 or bother the seriousness and consequences of COVID-19 at present. Until further information are accessible, it's miles encouraged that ARB and ACEI medications be endured for the remedy of patients with cardiovascular disease and hypertension, especially the ones at high risk, in step with guideline-directed clinical therapy based on the currently available evidence. [113-115]

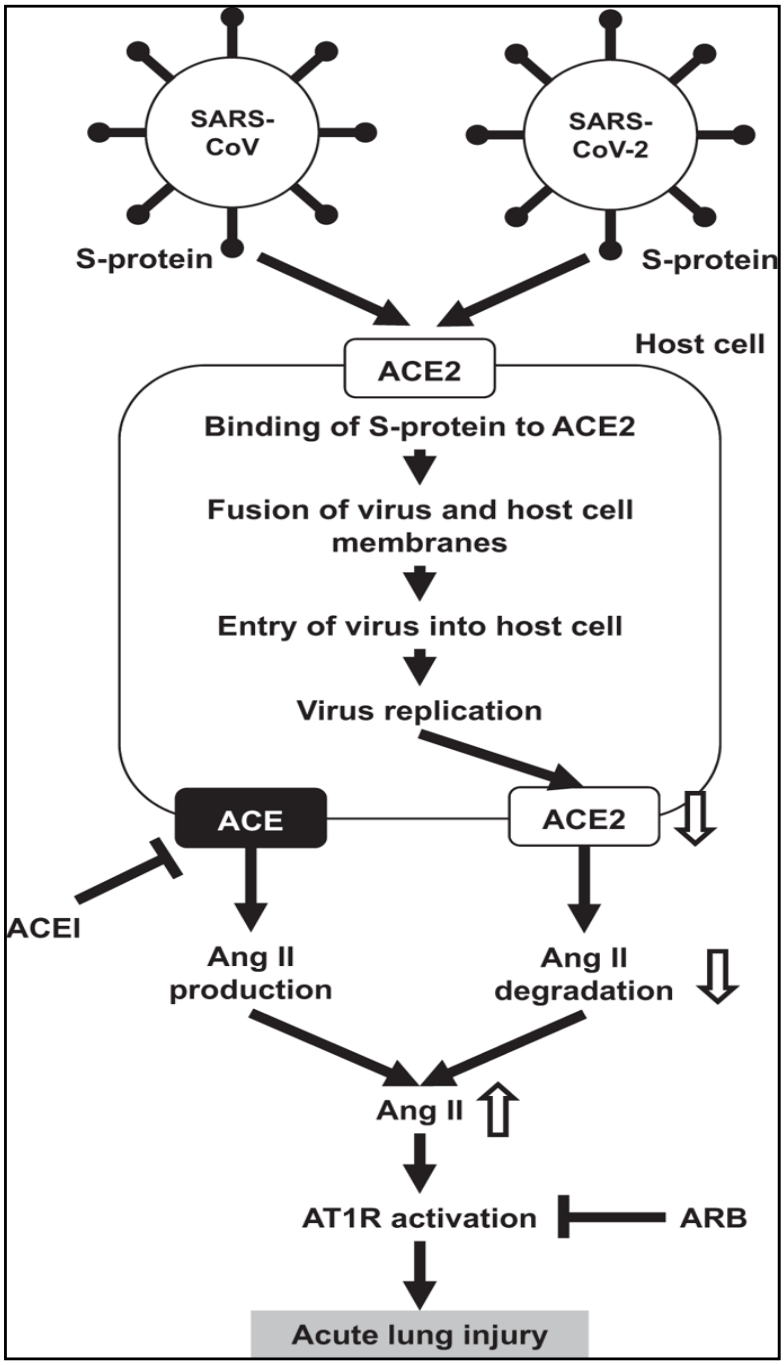

Figure 6. Conceivable plan of the relationship of ACE2, angiotensin II, and AT1R and intense lung injury of SARS and COVID-19. Ang II, angiotensin II; ACE, angiotensin-

changing over compound; ACE2, angiotensin-changing over chemical 2; ACEI, angiotensin-changing over catalyst inhibitor; AT1R, angiotensin II type-1 receptor; ARB, angiotensin II type-1 receptor blocker; SARS-CoV, serious intense respiratory disorder coronavirus; SARS-CoV-2, extreme intense respiratory condition coronavirus 2; S-protein, spike-glycoprotein.[116]

As of late, an Italian patient of COVID-19 is treated in Sawai Man Singh (SMS) Hospital, Jaipur India by giving a combination of lopinavir (200 mg) and ritonavir (50 mg) two times per day. In addition, the patient was additionally given a dose of oseltamivir and chloroquine medication. [117]

Asymptomatic 2019-coronavirus ailment tolerant (ten patients) with normal radiography all through showed up in an examination. Furthermore, it is observed that Lopinavir positively affects 2019-coronavirus ailment patients. Eosinophil count is noticed as a crucial bio-indicator of COVID-19 progression. Expanding eosinophils might be a pointer of COVID-19 improvement. The COVID-19 patients may profit by continued lopinavir administration. [118]

While generally speaking death rate is probably going to be lower than the present appraisals, as the pervasiveness of somewhat mildly symptomatic cases still cannot seem to be clearly characterized, COVID-19 has now become an obvious crisis for human civilization. There are no authorized vaccines or approved antiviral drug treatment to secure or treat against COVID-19. Antiviral treatment that viably captures infection and useful vaccines that ensure against extreme COVID-19 is along these lines critically required to meet medical and general wellbeing needs. An intermingling among medication and vaccine for Covid-19 is the harnessing of the invulnerable reaction to SARS CoV-2. To address these issues, different gatherings have made striking steps in bringing new therapeutics and vaccines into clinical advancement within a brief time-frame. [119-120]

Indian Status Report:

India is currently in a conclusive period of the reaction. As on account of polio, in fighting COVID-19 as well, reconnaissance is assuming a focal role. In like manner, in line with the government, WHO has additionally ventured up the help in fortifying continuous surveillance and reaction at state, region and block levels; group control exercises that is containment or

isolation zone; reinforcing ongoing information assortment exercises; and quickened usage of the national Integrated Health Information Platform.

As on 2 August 2020, 08:00 IST there were 567,730 Active Cases 1,145,629 Cured/Discharged, 1 Migrated and 37,364 Deaths in India. India's Case Fatality Rate (CFR) is its lowest at 2.15% since 1st Lockdown; Total recoveries nearly 11 lakh; [121]

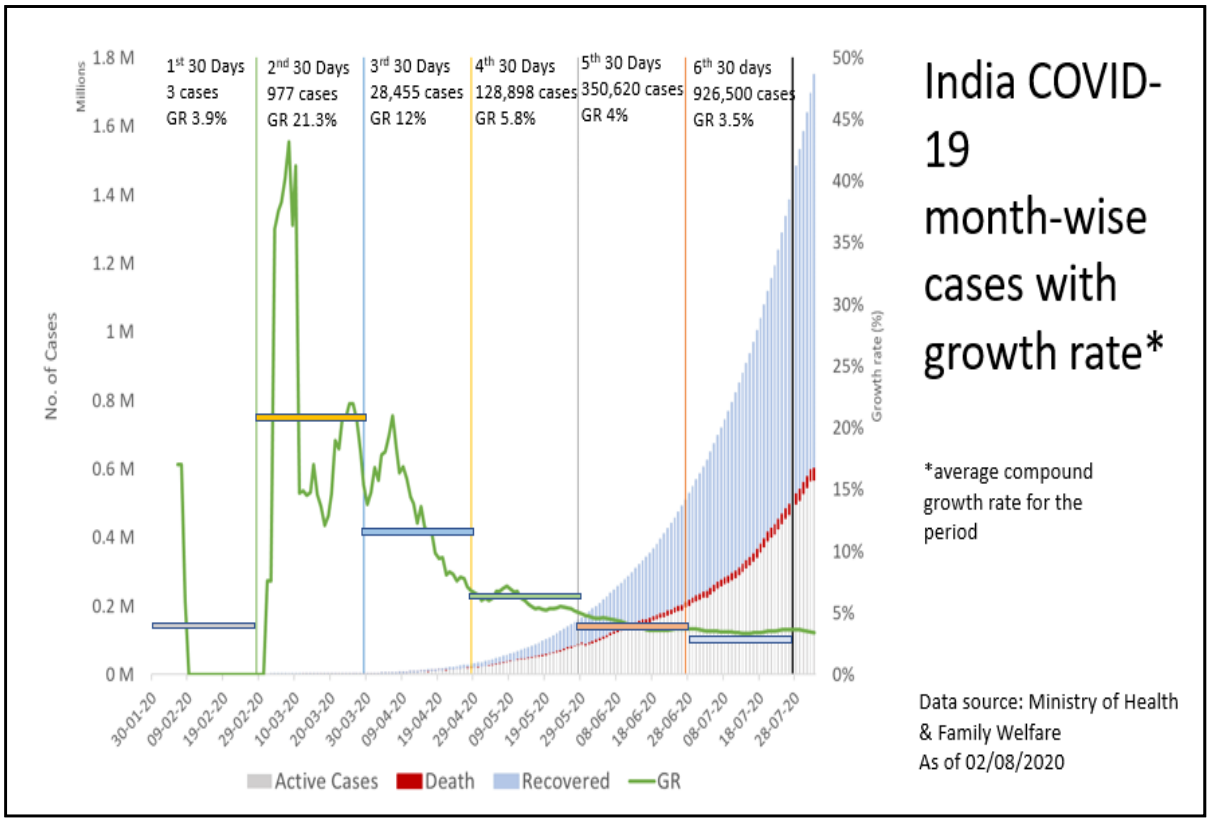

Figure 7. Graphical presentation of COVID-19 medical status in India.

Conclusion:

COVID-19 pandemic is a worldwide health crisis. It has presented new difficulties to the worldwide research fraternity. Broad research is required for the advancement of a vaccine for the avoidance of Coronavirus disease. There is a dire requirement for early production and assembling of the basic things like individual defensive hardware (personal protective equipment), medicines, and ventilators to battle this pandemic. All measures to keep a social separating by the public must be guaranteed by maintaining a strategic distance from social-traditional, religious programs and festivals etc during this pandemic. Alongside these, healthcare measures to manage COVID-19 pandemic, there is likewise an unavoidable

necessity for the research to improve the worldwide economy, which has taken a huge beating and is probably not going to recoup sooner rather than later.

Coronavirus (COVID-19) pandemic is developing exponentially in the entire world. Researchers, technologists, specialists and other healthcare laborers are working day and night on the evolution of vaccines and medicines to control and treat this infection. SARS-CoV-2 is the name of the infection liable for causing COVID-19 malady, which is exceptionally irresistible and deadly. With exponentially expanding diseases, proportionate fatalities are being accounted for both from developed and underdeveloped nations. Starting today, about 10 million individuals over the world have been accounted for contaminated with this infection, and in excess of 4 lakh individuals have kicked the bucket of this sickness. Consequently, there is a pressing prerequisite for directing scholastic research on a several aspects of this exceptionally infectious sickness, to discover compelling methods for control and treatment of the illness, for now and in future. We have recognized a few open doors for scholastic research pertaining to COVID-19 and have likewise given recommendations to contain forestalled and treat this viral disease.

With the assistance of academic research, there is a requirement for a superior comprehension of the COVID-19 and its socio-economic consequences on society. The future research will be multi-disciplinary and trans-national. We see another influx of research in the natural and the clinical sciences for the prosperity of the human advancement. This review will surely help to achieve and understand the above mentioned goals and tasks respectively.

References:

1. World Health Organization, South-East Asia Region, Western Pacific Region. Asia Pacific strategy for emerging diseases: 2010. New Delhi, Manila: WHO, South-East Asia Region, Western Pacific Region; 2011.

2. Mourya DT, Yadav PD, Ullas PT, Bhardwaj SD, Sahay RR, Chadha MS, Shete AM, Jadhav S, Gupta N, Gangakhedkar RR, Khasnobis P. Emerging/re-emerging viral diseases & new viruses on the Indian horizon. The Indian journal of medical research. 2019 Apr;149(4):447.]

3. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. The Lancet. 2020 Feb 15;395(10223):470-3.

4. Hussain YH, Baderkhan B, Hamid M, Hamid A. Mortalities and Morbidities Trends of COVID-19 Infection, From Explosiveness to Aggressiveness, Understanding Gaps in System Response and Transmission Chain Events. Journal of Health Care and Research. 2020;2020(1):22.

5. Mousavizadeh L, Ghasemi S. Genotype and phenotype of COVID-19: Their roles in pathogenesis. Journal of Microbiology, Immunology and Infection. 2020 Mar 31.

6. Raoult D, Zumla A, Locatelli F, Ippolito G, Kroemer G. Coronavirus infections: Epidemiological, clinical and immunological features and hypotheses. Cell Stress. 2020 Apr;4(4):66.

7. Kain T, Lindsay PJ, Adhikari NK, Arabi YM, Van Kerkhove MD, Fowler RA. Pharmacologic Treatments and Supportive Care for Middle East Respiratory Syndrome. Emerging Infectious Diseases. 2020 Mar 26;26(6).

8. Prasad S, Potdar V, Cherian S, Abraham P, Basu A, Team IN. Transmission electron microscopy imaging of SARS-CoV-2. Indian Journal of Medical Research. 2020 Feb 1;151(2):241.

9. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL, Chen HD. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. BioRxiv. 2020 Jan 1.

10. Halstead SB. An Urgent Need for" Common Cold Units" to Study Novel Coronavirus Disease (COVID-19). The American Journal of Tropical Medicine and Hygiene. 2020 Apr 9.

11. Speth RC. Response to recent commentaries regarding the involvement of a ngiotensin-converting enzyme 2 (ACE2) and renin-angiotensin system blockers in SARS-CoV-2 infections. Drug Development Research. 2020 Apr 17.

12. Wang Z, Xu X. scRNA-seq Profiling of Human Testes Reveals the Presence of the ACE2 Receptor, A Target for SARS-CoV-2 Infection in Spermatogonia, Leydig and Sertoli Cells. Cells. 2020 Apr;9(4):920.

13. Yan R, Zhang Y, Li Y, Xia L, Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. Science. 2020 Mar 27;367(6485):1444-8.

14. Hong N, Yu W, Xia J, Shen Y, Yap M, Han W. Evaluation of ocular symptoms and tropism of SARS-CoV-2 in patients confirmed with COVID-19. Acta Ophthalmologica. 2020 Apr 26.

15. Brufsky A. Distinct Viral Clades of SARS-CoV-2: Implications for Modeling of Viral Spread. Journal of Medical Virology. 2020 Apr 20.

16. Mothay D, Ramesh KV. Binding site analysis of potential protease inhibitors of COVID-19 using AutoDock. VirusDisease. 2020 May 2:1.

17. Chen Y, Guo Y, Pan Y, Zhao ZJ. Structure analysis of the receptor binding of 2019-nCoV. Biochemical and biophysical research communications. 2020 Feb 17.

18. Wrapp D, De Vlieger D, Corbett KS, Torres GM, Wang N, Van Breedam W, Roose K, van Schie L, COVID VC, Hoffmann M, Pöhlmann S. Structural Basis for Potent Neutralization of Betacoronaviruses by Single-domain Camelid Antibodies. Cell. 2020 May 5.

19. Fung SY, Yuen KS, Ye ZW, Chan CP, Jin DY. A tug-of-war between severe acute respiratory syndrome coronavirus 2 and host antiviral defence: lessons from other pathogenic viruses. Emerging microbes & infections. 2020 Jan 1;9(1):558-70.

20. Hoffmann M, Kleine-Weber H, Pöhlmann S. A multibasic cleavage site in the spike protein of SARS-CoV-2 is essential for infection of human lung cells. Molecular Cell. 2020 May 1.

21. Elfiky AA. Natural products may interfere with SARS-CoV-2 attachment to the host cell. Journal of Biomolecular Structure and Dynamics. 2020 Apr 27(just-accepted):1-6.

22. Ibrahim IM, Abdelmalek DH, Elshahat ME, Elfiky AA. COVID-19 spike-host cell receptor GRP78 binding site prediction. Journal of Infection. 2020 Mar 10.

23. Yadav PD, Potdar VA, Choudhary ML, Nyayanit DA, Agrawal M, Jadhav SM, Majumdar TD, Shete-Aich A, Basu A, Abraham P, Cherian SS. Full-genome sequences of the first two SARS-CoV-2 viruses from India. Indian Journal of Medical Research. 2020 Feb 1;151(2):200.

24. Potdar V, Cherian SS, Deshpande GR, Ullas PT, Yadav PD, Choudhary ML, Gughe R, Vipat V, Jadhav S, Patil S, Nyayanit D. Genomic analysis of SARS-CoV-2 strains among Indians returning from Italy, Iran & China, & Italian tourists in India. Indian Journal of Medical Research. 2020 Feb 1;151(2):255.

25. Zhang T, Wu Q, Zhang Z. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. Current Biology. 2020 Mar 19.

26. Li X, Song Y, Wong G, Cui J. Bat origin of a new human coronavirus: there and back again. Science China Life Sciences. 2020 Mar;63(3):461-2.

27. Li X, Zai J, Zhao Q, Nie Q, Li Y, Foley BT, Chaillon A. Evolutionary history, potential intermediate animal host, and cross-species analyses of SARS-CoV-2. Journal of medical virology. 2020 Feb 27.

28. Donaldson EF, Haskew AN, Gates JE, Huynh J, Moore CJ, Frieman MB. Metagenomic analysis of the viromes of three North American bat species: viral diversity among

different bat species that share a common habitat. Journal of virology. 2010 Dec 15;84(24):13004-18.

29. Maganga GD, Pinto A, Mombo IM, Madjitobaye M, Beyeme AM, Boundenga L, Gouilh MA, N'Dilimabaka N, Drexler JF, Drosten C, Leroy EM. Genetic diversity and ecology of coronaviruses hosted by cave-dwelling bats in Gabon. Scientific Reports. 2020 Apr 30;10(1):1-3.

30. Kassahun B, Berhanu T, Damtew B. Review on coronavirus, a middle east respiratory syndrome (MERS-CoV). Online J. Anim. Feed Res. 2020;10(1).

31. Salata C, Calistri A, Parolin C, Palu G. Coronaviruses: a paradigm of new emerging zoonotic diseases. Pathogens and disease. 2019 Dec;77(9):ftaa006.

32. Ye ZW, Yuan S, Yuen KS, Fung SY, Chan CP, Jin DY. Zoonotic origins of human coronaviruses. International journal of biological sciences. 2020;16(10):1686.

33. Danchin A, Timmis K. SARS-CoV-2 variants: relevance for symptom granularity, epidemiology, immunity (herd, vaccines), virus origin and containment?. Environmental Microbiology. 2020 May 4.

34. Wang R, Hozumi Y, Yin C, Wei GW. Decoding SARS-CoV-2 transmission, evolution and ramification on COVID-19 diagnosis, vaccine, and medicine. arXiv preprint arXiv:2004.14114. 2020 Apr 29.

35. Ji W, Wang W, Zhao X, Zai J, Li X. Cross-species transmission of the newly identified coronavirus 2019-nCoV. Journal of medical virology. 2020 Apr;92(4):433-40.

36. Khailany RA, Safdar M, Ozaslan M. Genomic characterization of a novel SARS-CoV-2. Gene Reports. 2020 Apr 16:100682.

37. Cagliani R, Forni D, Clerici M, Sironi M. Computational inference of selection underlying the evolution of the novel coronavirus, SARS-CoV-2. Journal of Virology. 2020 Apr 1.

38. Shafique L, Ihsan A, Liu Q. Evolutionary trajectory for the emergence of novel coronavirus SARS-CoV-2. Pathogens. 2020 Mar;9(3):240.

39. Sun J, He WT, Wang L, Lai A, Ji X, Zhai X, Li G, Suchard MA, Tian J, Zhou J, Veit M. COVID-19: epidemiology, evolution, and cross-disciplinary perspectives. Trends in Molecular Medicine. 2020 Mar 21.

40. Gralinski LE, Baric RS. Molecular pathology of emerging coronavirus infections. The Journal of pathology. 2015 Jan;235(2):185-95.

41. Cyranoski D. Profile of a killer: the complex biology powering the coronavirus pandemic. Nature. 2020 May 1;581(7806):22-6.

42. Yaqinuddin A, Kashir J. Innate immunity in COVID-19 patients mediated by NKG2A receptors, and potential treatment using Monalizumab, Cholroquine, and antiviral agents. Medical Hypotheses. 2020 Apr 22:109777.

43. Kasibhatla SM, Kinikar M, Limaye S, Kale MM, Kulkarni-Kale U. Understanding evolution of SARS-CoV-2: a perspective from analysis of genetic diversity of RdRp gene. Journal of Medical Virology. 2020 Apr 21.

44. Lockwood W. Coronavirus Infections: SARS, MERS, and COVID-19 WWW. RN. ORG®.

45. Hou Z, Lin L, Lu L, Du F, Qian M, Liang Y, Zhang J, Yu H. Public Exposure to Live Animals, Behavioural Change, and Support in Containment Measures in response to COVID-19 Outbreak: a population-based cross sectional survey in China. medRxiv. 2020 Jan 1.

46. Shen W, Zhang Y, Zhang D. Simple Legislative Declaration and Complex Cultural Background: Review of China's Legal Response to the COVID-19. Michigan International Lawyer Michigan Internatioichigan International Lawyer.:3.

47. Lu S, Lin J, Zhang Z, Xiao L, Jiang Z, Chen J, Hu C, Luo S. Alert for non-respiratory symptoms of Coronavirus Disease 2019 (COVID-19) patients in epidemic period: A case report of familial cluster with three asymptomatic COVID-19 patients. Journal of medical virology. 2020 Mar 19.

48. Wang Y, Liu Y, Liu L, Wang X, Luo N, Ling L. Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China. The Journal of infectious diseases. 2020 Mar 17.

49. Lippi G, Simundic AM, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19). Clinical Chemistry and Laboratory Medicine (CCLM). 2020 Mar 16;1(ahead-of-print).

50. Rahimi F, Abadi AT. Challenges of managing the asymptomatic carriers of SARS-CoV-2. Travel Medicine and Infectious Disease. 2020 Apr 18:101677.

51. Khan MM, Parab SR. Safety Guidelines for Sterility of Face Shields During COVID 19 Pandemic. Indian Journal of Otolaryngology and Head & Neck Surgery. 2020 Apr 30:1.

52. Li Y, Ren B, Peng X, Hu T, Li J, Gong T, Tang B, Xu X, Zhou X. Saliva is a non-negligible factor in the spread of COVID-19. Molecular Oral Microbiology. 2020 May 4.

53. Zhang J, Wu S, Xu L. Asymptomatic carriers of COVID-19 as a concern for disease prevention and control: more testing, more follow-up. Bioscience trends. 2020 Apr 22.

54. Balkhair AA. COVID-19 Pandemic: A New Chapter in the History of Infectious Diseases. Oman Medical Journal. 2020 Mar;35(2):e123.

55. Werner C, Scullen T, Mathkour M, Zeoli T, Beighley A, Kilgore MD, Carr C, Zweifler RM, Aysenne A, Maulucci CM, Dumont AS. Neurological Impact of Coronavirus Disease (COVID-19): Practical Considerations for the Neuroscience Community. World Neurosurgery. 2020 May 6.

56. Rossi PG, Broccoli S, Angelini P, Emilia-Romagna COVID-19 working group. Case fatality rate in patients with COVID-19 infection and its relationship with length of follow up. Journal of Clinical Virology. 2020 May 5.

57. Gheblawi M, Wang K, Viveiros A, Nguyen Q, Zhong JC, Turner AJ, Raizada MK, Grant MB, Oudit GY. Angiotensin-Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System: Celebrating the 20th Anniversary of the Discovery of ACE2. Circulation research. 2020 May 8;126(10):1456-74.

58. Yang X, Zhao J, Yan Q, Zhang S, Wang Y, Li Y. A case of COVID-19 patient with the diarrhea as initial symptom and literature review. Clinics and Research in Hepatology and Gastroenterology. 2020 Apr 15.

59. Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. BMJ (Clinical research ed.). 2020 Mar 26;368:m1198.

60. Stein RA. COVID-19 and rationally layered social distancing. International Journal of Clinical Practice. 2020 Mar 14:e13501.

61. Wang D, Ju XL, Xie F, Lu Y, Li FY, Huang HH, Fang XL, Li YJ, Wang JY, Yi B, Yue JX. Clinical analysis of 31 cases of 2019 novel coronavirus infection in children from six provinces (autonomous region) of northern China. Zhonghua er ke za zhi= Chinese journal of pediatrics. 2020 Mar 2;58(4):E011-.

62. Robert Koch Institute (RKI) (2020) Epidemiologisches Bulletin 17/2020. https://www.rki.de/DE/ Content/Infekt/EpidBull/Archiv/2020/Ausgaben/ Herz 17_20.pdf?__blob=publicationFile;. Accessed 30 Apr2020}

63. Pathak M, Patel SK, Jigyasa R, Tiwari R, Dhama K, Sah R, Rabaan AA, Bonilla-Aldana DK, Rodriguez-Morales AJ. Global Threat of SARS-CoV-2/COVID-19 and the Need for More and Better Diagnostic Tools. Archives of Medical Research. 2020 Apr 15.

64. Kadry S, Rajinikanth V, Rho S, Raja NS, Rao VS, Thanaraj KP. Development of a Machine-Learning System to Classify Lung CT Scan Images into Normal/COVID-19 Class. arXiv preprint arXiv:2004.13122. 2020 Apr 24.

65. Castelnuovo P, Turri-Zanoni M, Karligkiotis A, Battaglia P, Pozzi F, Locatelli D, Bernucci C, Iacoangeli M, Krengli M, Marchetti M, Pareschi R. Skull base surgery during the Covid-19 pandemic: The Italian skull base society recommendations. InInternational Forum of Allergy & Rhinology 2020 Apr 29.

66. Ramírez-Mora T, Retana-Lobo C, Reyes-Carmona J. COVID-19: Perspectives on the Pandemic and its Incidence in Dentistry. Odovtos-International Journal of Dental Sciences. 2020 May 6:25-45.

67. Shen M, Zhou Y, Ye J, AL-maskri AA, Kang Y, Zeng S, Cai S. Recent advances and perspectives of nucleic acid detection for coronavirus. Journal of Pharmaceutical Analysis. 2020 Mar 1.

68. Gutiérrez AB, Rodríguez-Morales AJ, Mejía ÁJ, Peña ÁA, Montoya ÁM, Muñoz AJ, García AL, Serrano AV, Escobar BP, Medina CA, González CA. Colombian consensus recommendations for diagnosis, management and treatment of the infection by SARS-COV-2/COVID-19 in health care facilities-Recommendations from expert´ s group based and informed on evidence. Infectio. 2020 Jan 1;24.

69. Kim H, Hong H, Yoon SH. Diagnostic performance of CT and reverse transcriptase-polymerase chain reaction for coronavirus disease 2019: a meta-analysis. Radiology. 2020 Apr 17:201343.

70. Lowe CF, Matic N, Ritchie G, Lawson T, Stefanovic A, Champagne S, Leung V, Romney MG. Detection of low levels of SARS-CoV-2 RNA from nasopharyngeal swabs using three commercial molecular assays. Journal of Clinical Virology. 2020 Apr 28:104387.

71. Loeffelholz MJ, Alland D, Butler-Wu SM, Pandey U, Perno CF, Nava A, Carroll KC, Mostafa H, Davies E, McEwan A, Rakeman JL. Multicenter Evaluation of the Cepheid Xpert Xpress SARS-CoV-2 Test. Journal of Clinical Microbiology. 2020 May 4.

72. Harrington A, Cox B, Snowdon J, Bakst J, Ley E, Grajales P, Maggiore J, Kahn S. Comparison of Abbott ID Now and Abbott m2000 methods for the detection of SARS-CoV-2 from nasopharyngeal and nasal swabs from symptomatic patients. Journal of Clinical Microbiology. 2020 Apr 23.

73. Lieberman JA, Pepper G, Naccache SN, Huang ML, Jerome KR, Greninger AL. Comparison of Commercially Available and Laboratory Developed Assays for in vitro Detection of SARS-CoV-2 in Clinical Laboratories. Journal of Clinical Microbiology. 2020 Apr 29.

74. Zhen W, Smith E, Manji R, Schron D, Berry GJ. Clinical Evaluation of Three Sample-To-Answer Platforms for the Detection of SARS-CoV-2. Journal of Clinical Microbiology. 2020 Apr 24.

75. Broughton JP, Deng X, Yu G, Fasching CL, Servellita V, Singh J, Miao X, Streithorst JA, Granados A, Sotomayor-Gonzalez A, Zorn K. CRISPR–Cas12-based detection of SARS-CoV-2. Nature Biotechnology. 2020 Apr 16:1-5.

76. Abbott TR, Dhamdhere G, Liu Y, Lin X, Goudy L, Zeng L, Chemparathy A, Chmura S, Heaton NS, Debs R, Pande T. Development of CRISPR as an antiviral strategy to combat SARS-CoV-2 and influenza. Cell. 2020 Apr 29.

77. Han Y, Chen T, Bryant J, Bucciarelli-Ducci C, Dyke C, Elliott MD, Ferrari VA, Friedrich MG, Lawton C, Manning WJ, Ordovas K. Society for Cardiovascular Magnetic Resonance (SCMR) guidance for the practice of cardiovascular magnetic resonance during the COVID-19 pandemic. Journal of cardiovascular magnetic resonance: official journal of the Society for Cardiovascular Magnetic Resonance. 2020 Apr 27;22(1):26.

78. Potdar V, Cherian SS, Deshpande GR, Ullas PT, Yadav PD, Choudhary ML, Gughe R, Vipat V, Jadhav S, Patil S, Nyayanit D. Genomic analysis of SARS-CoV-2 strains among Indians returning from Italy, Iran & China, & Italian tourists in India. Indian Journal of Medical Research. 2020 Feb 1;151(2):255.

79. Khan Z, Karataş Y, Rahman H. Anti COVID-19 Drugs: Need for More Clinical Evidence and Global Action. Advances in Therapy. 2020 Apr 29:1.

80. Baretić M. Case report of chloroquine therapy and hypoglycaemia in type 1 diabetes: What should we have in mind during the COVID-19 pandemic?. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020 Apr 13.

81. van den Broek MP, Möhlmann JE, Abeln BG, Liebregts M, van Dijk VF, van de Garde EM. Chloroquine-induced QTc prolongation in COVID-19 patients. Netherlands Heart Journal. 2020 Apr 29:1.

82. Gbinigie K, Frie K. Should chloroquine and hydroxychloroquine be used to treat COVID-19? A rapid review. BJGP open. 2020 Apr 8.

83. Dousa KM, Malavade SS, Furin J, Gripshover B, Hatszegi M, Hojat L, Saade E, Salata RA. SARS-CoV-2 infection in a patient on chronic hydroxychloroquine therapy: Implications for prophylaxis. IDCases. 2020 Apr 27:e00778.

84. Mack HG. Hydroxychloroquine use during the COVID-19 pandemic 2020. Australian Journal of General Practice. 2020 Apr 14;49.

85. DeJong C, Wachter RM. The Risks of Prescribing Hydroxychloroquine for Treatment of COVID-19—First, Do No Harm. JAMA Internal Medicine. 2020 Apr 29.

86. Singh AK, Singh A, Shaikh A, Singh R, Misra A. Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: A systematic search and a narrative review with a special reference to India and other developing countries. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020 Mar 26.

87. Zhu Z, Lu Z, Xu T, Chen C, Yang G, Zha T, Xue Y. Arbidol monotherapy is superior to lopinavir/ritonavir in treating COVID-19. Journal of Infection. 2020 Apr 10.

88. Liu F, Xu A, Zhang Y, Xuan W, Yan T, Pan K, Yu W, Zhang J. Patients of COVID-19 may benefit from sustained lopinavir-combined regimen and the increase of eosinophil may predict the outcome of COVID-19 progression. International Journal of Infectious Diseases. 2020 Mar 12.

89. Stower H. Lopinavir–ritonavir in severe COVID-19. Nature Medicine. 2020 Apr 9:1-.

90. Yin W, Mao C, Luan X, Shen DD, Shen Q, Su H, Wang X, Zhou F, Zhao W, Gao M, Chang S. Structural basis for inhibition of the RNA-dependent RNA polymerase from SARS-CoV-2 by remdesivir. Science. 2020 May 1.

91. Cao YC, Deng QX, Dai SX. Remdesivir for severe acute respiratory syndrome coronavirus 2 causing COVID-19: An evaluation of the evidence. Travel Medicine and Infectious Disease. 2020 Apr 2:101647.

92. Kirchdoerfer RN. Halting coronavirus polymerase. Journal of Biological Chemistry. 2020 Apr 10;295(15):4780-1.

93. Ferner RE, Aronson JK. Remdesivir in covid-19. BMJ (Clinical research ed.). 2020 Apr 22;369:m1610.

94. Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y, Fu S, Gao L, Cheng Z, Lu Q, Hu Y. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. The Lancet. 2020 Apr 29.

95. Costanzo M, De Giglio MA, Roviello GN. SARS CoV-2: Recent Reports on Antiviral Therapies Based on Lopinavir/Ritonavir, Darunavir/Umifenovir, Hydroxychloroquine, Remdesivir, Favipiravir and Other Drugs for the Treatment of the New Coronavirus. Current medicinal chemistry. 2020 Apr 16.

96. Harismah K, Mirzaei M. Favipiravir: Structural Analysis and Activity against COVID-19. Advanced Journal of Chemistry, Section B: Natural Products and Medical Chemistry. 2020 Jun 1;2(2):55-60.

97. Du YX, Chen XP. Favipiravir: pharmacokinetics and concerns about clinical trials for 2019-nCoV infection. Clinical Pharmacology & Therapeutics. 2020 Apr 4.

98. Costanzo M, De Giglio MA, Roviello GN. SARS CoV-2: Recent Reports on Antiviral Therapies Based on Lopinavir/Ritonavir, Darunavir/Umifenovir, Hydroxychloroquine, Remdesivir, Favipiravir and Other Drugs for the Treatment of the New Coronavirus. Current medicinal chemistry. 2020 Apr 16.

99. Seneviratne SL, Abeysuriya V, de Mel S, De Zoysa I, Niloofa R. Favipiravir in Covid-19.

100. Sarayani A, Cicali B, Henriksen CH, Brown JD. Safety signals for QT prolongation or Torsades de Pointes associated with azithromycin with or without chloroquine or hydroxychloroquine. Research in Social and Administrative Pharmacy. 2020 Apr 19.

101. Saleh M, Gabriels J, Chang D, Kim BS, Mansoor A, Mahmood E, Makker P, Ismail H, Goldner B, Willner J, Beldner S. The Effect of Chloroquine, Hydroxychloroquine and Azithromycin on the Corrected QT Interval in Patients with SARS-CoV-2 Infection. Circulation: Arrhythmia and Electrophysiology. 2020 Apr 29.

102. Damle B, Vourvahis M, Wang E, Leaney J, Corrigan B. Clinical Pharmacology Perspectives on the Antiviral Activity of Azithromycin and Use in COVID-19. Clinical Pharmacology & Therapeutics. 2020 Apr 17.

103. Gritti G, Raimondi F, Ripamonti D, Riva I, Landi F, Alborghetti L, Frigeni M, Damiani M, Micò C, Fagiuoli S, Cosentini R. Use of siltuximab in patients with COVID-19 pneumonia requiring ventilatory support. medRxiv. 2020 Jan 1.

104. Zhang J, Xie B, Hashimoto K. Current status of potential therapeutic candidates for the COVID-19 crisis. Brain, Behavior, and Immunity. 2020 Apr 22.

105. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020 Apr 9.

106. Helmy YA, Fawzy M, Elaswad A, Sobieh A, Kenney SP, Shehata AA. The COVID-19 Pandemic: A Comprehensive Review of Taxonomy, Genetics, Epidemiology, Diagnosis, Treatment, and Control. Journal of Clinical Medicine. 2020 Apr;9(4):1225.

107. Philippidis A. COVID-19: Top 60 Drug Treatments in Development: The biopharma industry is ramping up the development of dozens of potential drug therapies and clinical testing in an all-hands effort to combat the pandemic. Genetic Engineering & Biotechnology News. 2020 Apr 1;40(4):10-3.

108. Lambert CG, Stoicu S, Nestsiarovich A, Kumar P, Myers O, Rowland AS, Raballah E, Munde E, Anyona S, King RD, Groves H. 2020-04-13 DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING.

109. Brown BL, McCullough J. TreaTment for emerging viruses: Convalescent plasma and COVID-19. Transfusion and Apheresis Science. 2020 Apr 20:102790.

110. Keil SD, Ragan I, Yonemura S, Hartson L, Dart NK, Bowen R. Inactivation of severe acute respiratory syndrome coronavirus 2 in plasma and platelet products using a riboflavin and ultraviolet light-based photochemical treatment. Vox Sanguinis. 2020 Apr 20.

111. Özdemir Ö, Melek Arsoy HE. Convalescent (Immune) Plasma Therapy with all Aspects: Yesterday, Today and COVID-19. ERCİYES MEDICAL JOURNAL. 2020 Apr 20;42.

112. Syal K. COVID-19: Herd Immunity and Convalescent Plasma Transfer Therapy. Journal of Medical Virology. 2020 Apr 13.

113. Katsiki N, Banach M, Mikhailidis DP. Lipid-lowering therapy and renin-angiotensin-aldosterone system inhibitors in the era of the COVID-19 pandemic. Arch Med Sci. 2020;16(3):485-9.

114. Javanmard SH, Heshmat-Ghahdarijani K, Vaseghi G. Angiotensin-converting-enzyme inhibitors (ACE inhibitors) and Angiotensin II receptor blocker (ARB) Use in COVID-19 prevention or treatment: A Paradox. Infection Control & Hospital Epidemiology. 2020 May 4:1-5.

115. Saavedra JM. Angiotensin Receptor Blockers and 2019-nCoV. Pharmacological Research. 2020 Apr 15:104832.

116. Kai H, Kai M. Interactions of coronaviruses with ACE2, angiotensin II, and RAS inhibitors—lessons from available evidence and insights into COVID-19. Hypertension Research. 2020 Apr 27:1-7.

117. Ali I, Alharbi OM. COVID-19: Disease, management, treatment, and social impact. Science of the Total Environment. 2020 Apr 22:138861.

118. Liu F, Xu A, Zhang Y, Xuan W, Yan T, Pan K, Yu W, Zhang J. Patients of COVID-19 may benefit from sustained lopinavir-combined regimen and the increase of eosinophil may predict the outcome of COVID-19 progression. International Journal of Infectious Diseases. 2020 Mar 12.

119. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, Zimmer T, Thiel V, Janke C, Guggemos W, Seilmaier M. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. New England Journal of Medicine. 2020 Mar 5;382(10):970-1.

120. de Alwis R, Chen S, Gan ES, Ooi EE. Impact of immune enhancement on Covid-19 polyclonal hyperimmune globulin therapy and vaccine development. EBioMedicine. 2020 Apr 16:102768.

121. https://www.who.int/india/emergencies/coronavirus-disease-(covid-19)/india-situation-report, assessed on 5-August-2020