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A novel coronavirus (SARS-CoV-2): current status and challenges

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ABSTRACT: In December, 2019 a new public health crisis threatened the world with the emergence of new zoonotic virus, the 2019 novel coronavirus. SARS-CoV-2 or severe acute respiratory syndrome coronavirus-2 belongs to the family of coronaviruses named for the crown-like spikes on its surfaces. SARS-CoV-2 causes COVID-19 (Coronavirus Disease-2019), a contagious viral infection that attacks primarily throat and lungs causing pneumonia-like symptoms. It is speculated that SARS-CoV-2 seem to have come from a bat, but the intermediate reservoir is still unknown. This review will address SARS-CoV-2 structure, clinical features, SARS-CoV-2 genome and its different variant, diagnosis, and treatment and also gives a bird's eye view on the epidemiology and pathology based on current evidence.

Keywords: Coronavirus; COVID-19; SARS-CoV-2; Variant; ACE-2; Vaccines; Genome.

1. INTRODUCTION

In the past two decades, several infectious diseases such as Influenza (H1N1), Ebola, SARS, and MERS have affected the world, which have had a strain on the global public health and economy [1,2]. In 2002, Severe Acute Respiratory Syndrome (SARS) in China and in 2012, Middle East Respiratory Syndrome (MERS) in Saudi Arabia astonished the world [1]. At the end of the year 2019, a new zoonotic Coronavirus occurred in Wuhan, Hubei province, China, caused an unknown infectious disease with pneumonia-like symptoms in humans. The causative agent of this disease was identified as novel coronavirus. This virus was named by WHO as sever acute respiratory syndrome coronavirus-2 (SARS-CoV-2) or novel coronavirus-2019 (2019-nCov), causing the disease coronavirus disease-2019 (COVID-19) [1,2].

In India, the first case of COVID-19 was reported in Kerala on January 27, 2020 in the infected person who had returned from Wuhan, China [3]. Till April 29, 2021 around 14,97,44,454 confirmed global cases of COVID-19 and 31,53,526 deaths have been reported and In India 1,85,52,408 confirmed cases and 2,05,968 deaths have been reported. However, 1,51,88,830 patients in India and 8,58,79,081 patients across the world have recovered from the disease [4]. On March 11, 2020 the World Health Organization declared the COVID-19 outbreak a pandemic [5].

2. HISTORY

The coronaviruses are zoonotic viruses. Coronavirus belongs to a group of highly diverse enveloped (60 nm to 140 nm in diameter), positive-sense, single stranded RNA virus [1,2]. Its genome ranges from 26 to 32 kilobases in size [6]. This size of genome of coronavirus leads to greater possibilities of errors, resulting in very rapid mutation and by these mutations the virus gets ability to infect new types of cells, generating serious lung diseases [7]. Four coronaviruses HCoV-OC43, HCoV-229E, HCoV-NL63, and HCoV-HKU1, generally infect human and cause mild respiratory diseases [8,9]. SARS-CoV-2 belongs to the B-lineage of the beta-coronavirus [9]. In 2002, a new coronavirus of the beta-lineage of bat origin infected human in the Guangdong province of China. Palm civet cat served as intermediate host for virus. The virus was designated as Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), with mortality rate around 10%. In 2012, the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), also of bat origin, infected people in Saudi Arabia with mortality rate around 35% [10,11].

3. CORONAVIRUS CHARACTERISTICS

A coronavirus particle consists of four structural proteins: the nucleocapsid (N) protein, membrane (M) protein, spike (S) protein, and envelope (E) protein, along with several non-structural proteins (nsp) [12]. The spike proteins glycoprotein, with a large molecular weight of 1,273 amino acids form club shaped protrusions over the surface, which resembles a crown hence the name, coronavirus (Figure 1). The specificity and host range for the virus is determined by their spike proteins. The most abundant protein of the virus surface is M protein. M-protein plays an important role of central organizer for assembly of virus [13] along with the envelope protein which is important for virus assembly [14]. The viral genetic material is encapsulated by lipid envelope. Hemagglutinin-esterase (HE) dimer has been located on the surface of virus which may be involved in entry of virus into host cell [15-17].

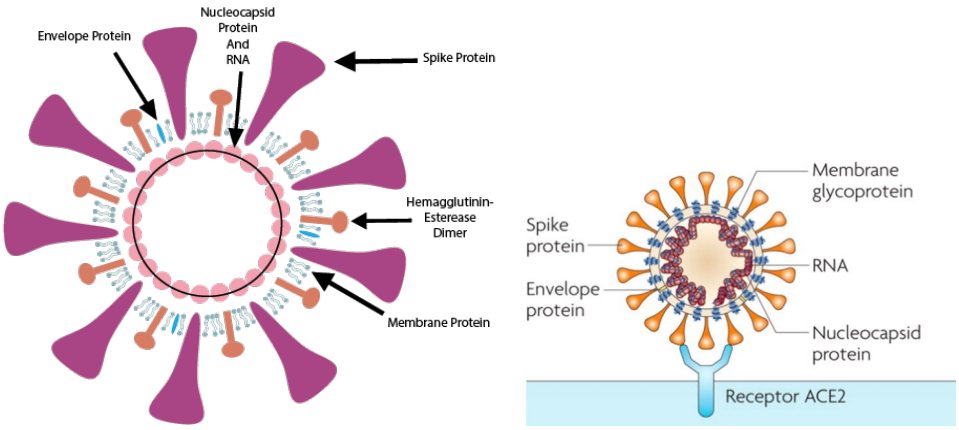

Figure 1. Schematic representation of SARS-CoV-2 structure and Coronavirus structure with receptor ACE2.

As other viruses, SARS-CoV-2 enters into the epithelial cells of lung alveoli using receptor mediated endocytosis [18]. The S-protein has two functional domains: S1 domain, responsible for receptor binding and S2 domain, which is responsible for membrane fusion of virus and host cell [19,20]. SARS-CoV-2 enters epithelial cells in the mucosal membrane (eyes, nose, and mouth) or the respiratory tract. As in SARS-CoV infection during entry of virus the spike glycoprotein of SARS-CoV-2 attaches to the Angiotensin Converting

Enzyme-2 (ACE-2) protein, which is found on host cell and mostly distributed on ciliated epithelial cells of lower bronchi [21-24].

In coronaviruses including omicron variant, SARS-CoV-2 is activated by TMPRSS2 and can thus be inhibited by TMPRSS2 inhibitors. In SARS-CoV-2 uses the SARS-CoV receptor ACE-2 for entry and the serine protease TMPRSS2 for S protein priming. The S protein consists of a transmembrane domain disulfide bonded extracellular N-terminus, and a short intracellular C-terminal part with palmitoylation [25]. The S protein plays major role of host immune response (HIR), and is involved in viral pathogenesis through activation of endoplasmic reticulum (ER) stress response [25,26].

Yadav et al. [27] reported that there are nine accessory proteins - ORF3a, 3d, 6, 7a, 7b, 8, 9b, 14, and 10. Out of these 3a is encoded by ORF3a located in between the S and E genes which is the largest proteins of SARS-CoV-2 consisting of 274 amino acids. Furthermore SARS-CoV ORF6 protein is consisting of a 61-amino acid long membrane-associated protein. The ORF7b protein consists of 44-amino acids whereas ORF8 is one of the youngest genes, shows low homology to SARS-CoV. This protein consists of 121 amino acid residues. Another accessory protein ORF9b consists of 97 amino acid residues, and is probably expressed by leaky scanning of sgRNA of N gene. ORF14 Protein is made up of 73 amino acid and is also likely to be synthesized by sgRNA of N gene [27].

Thus virus enters the host cell by endocytosis which is mediated by the spike proteins on the virus surface and ACE-2 receptor on host cells (Figure 2). The cell surface protease TMPRSS2 and lysosomal protease cathepsins are essential for the entry of virus into host cell and fusion with endosome and release of viral nucleoprotein in host cell cytoplasm, respectively [28]. Due to thinner respiratory fluid lining, ACE-2 receptor in alveolar epithelium is more accessible to the pathogen and facilitates infection [17,29].

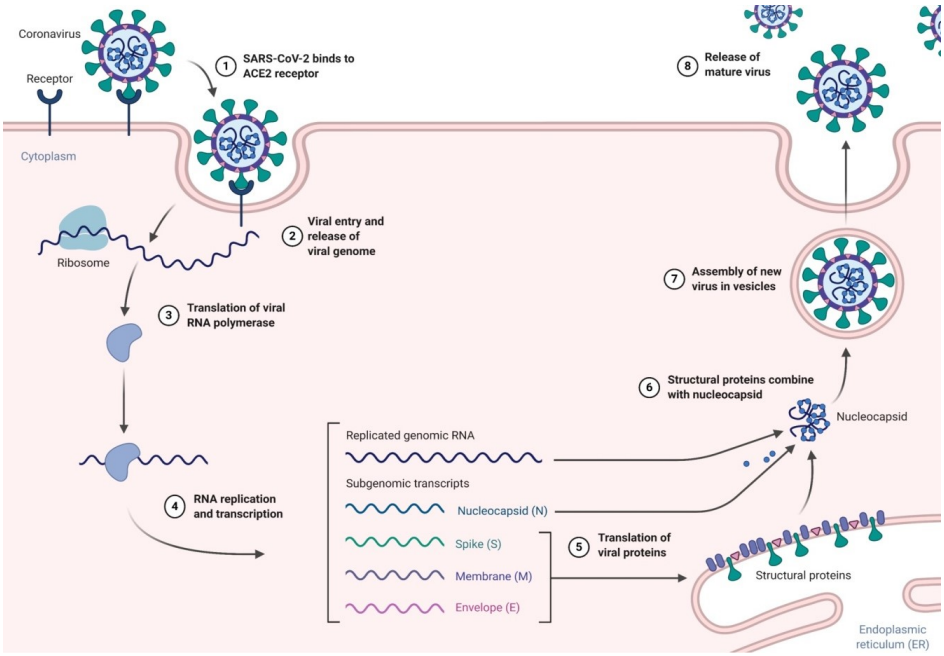

Figure 2. Schematic representation of SARS-CoV-2 life cycle. S-protein binds to host cellular receptor ACE2. After fusion of host cell and viral plasma membrane, viral genome undergoes replication and transcription. Viral RNA and proteins are subsequently arranged into new virus particles in ER and Golgi followed by budding into the lumen of the ERGIC. New virions are released into vesicles. ACE2, angiotensin-converting enzyme 2; ER, endoplasmic reticulum; ERGIC, endoplasmic reticulum-Golgi intermediate compartment. Source: https://www.wikidoc.org/index.php/SARS-CoV-2

4. CLINICAL SYMPTOMS

The clinical feature of COVID-19 ranges from asymptomatic state to acute and severe respiratory failure. Some common symptoms are fever, fatigue, dry cough and dyspnea [30]. Based on severity of symptoms, COVID-19 patients can be classified into three clinical types: mild type, which show non pneumonia or mild pneumonia symptom; severe type showing dyspnea, respiratory frequency ≥30/min, blood oxygen saturation <93%; lung infiltration ≥50% within 24/48 hours; and critical type showing symptoms like respiratory failure, septic shock, and/or multiple organ dysfunction or failure [31]. The incubation period of SARS-CoV-2 ranges within 2-14 days [32].

Kaushik and Singh [33] mentioned that the radiographic features of coronaviruses are similar to those which are found in community-acquired pneumonia caused by some other organisms. The most important tool to diagnose this pneumonia is computed tomography (CT) scan. A recent study observed that most of the patients about (90%) had bilateral chest CT findings, and the sensitivity of chest CT to suggest COVID-19 was 97%. Having chest CT imaging features with clinical symptoms could facilitate early diagnosis of COVID-19 pneumonia. If we compare with bacterial pneumonia, patients with COVID-19 had a lower oxygenation index. Laboratory observations states that 82.1% of patients were lymphopenia and 36.2% of patients were thrombocytopenic.

5. DIAGNOSIS

Although all age groups are susceptible to this disease, studies suggest that the patients >60 years of age are highly susceptible for COVID-19 infection than the children [30]. Patients with comorbidities such as diabetes, hypertension, and cardiovascular and pulmonary disease are under the threat of infection with severity of the disease [30] and case fatality rate is also high in these patients.

The easy diagnosis of COVID-19 can be done by tracing a good contact history and systemic symptoms. But the clinical diagnosis in laboratories is more reliable. Now the days, number of detection methods is being used in laboratories for diagnosis of COVID-19. One of the most reliable clinical testing for COVID-19 is RT-PCR (Reverse Transcriptase Polymerase Chain Reaction). For detection of pathogen in nasopharyngeal swab, different genes and primers are being tested by RT-PCR method according WHO protocol. Different RT-PCR designed kits detect for different genes such as E gene, RNA Dependent RNA polymerase (RdRp) gene, ORF 1ab gene, N genes, ORF 1b-nsp14 and spike protein gene [34]. Besides RT-PCR, antigen-antibody based serological tests and CT (Computed Topography) imaging of chest is also used for diagnosis of COVID-19 infection [33,35].

6. EPIDEMIOLOGY

Evidences from number of studies suggest that the transmission of coronavirus is human to human usually via airborne droplets generated during coughing and sneezing. Both symptomatic and asymptomatic patients can transmit the virus. Besides inhalation of the droplets, the infection is also acquired by touching contaminated surface and then touching nose or mouth [36]. SARS-CoV-2 has also been detected in tears [37].

7. IS CORONAVIRUS AIRBORNE?

The transmission is primarily based on direct or indirect spread of droplets generated by coughing and sneezing [38]. However, airborne spread of coronavirus is a topic of further detailed researches. Although,

evidences are limited but suggest that the airborne transmission of SARS-CoV-2 is possible. SARS-CoV-2 can pass from person to person in form of tiny droplets, called aerosol ranging <5 μm in diameter [38]. The collection of samples of aerosol in and around hospitals, treating COVID-19 patients by KeLan at Wuhan University strongly supports the airborne transmission of coronavirus [39].

The virus can remain viable on different surfaces for days in favourable conditions. On paper, virus can remain viable for 24 hours, 2 days on disposable gown and 24 hours on cotton gown [40], 2 days on glass and 4 days on plastic [41]. Some common disinfectants like sodium hypochlorite, hydrogen peroxide, detergent and alcohol based sanitizers can destroy the virus within a minute [1].

8. SARS-COV-2 GENOME

The first genome sequence of SARS-CoV-2 became available on the GISAID (Global Initiation on Sharing All Influenza Data) [42] and was named as the original virus from Wuhan (WIV 04 reference or hCoV-19/Wuhan/WIV04/2019) [42]. Genetically, SARS-CoV-2 has second largest genome of all RNA viruses having 5` cap 3` ploy-A tail. Final sequenced genome of SARS-CoV-2 consists of single, positive stranded RNA which is 29,811 nucleotides in length [43,44] having 8903 (29.86%) adenosines, 5482 (18.39%) cytocines, 5852 (19.63%) guanines and 9,574 (32.11%) thymines [44,45].

Genome of SARS-CoV-2 consists of 15 ORFs (Open Reading Frames) that encode 29 proteins [46]. The gene order is 5`-replicase ORF1ab-S-E-M-N-3` [44]. At the 5` terminal of the genome ORF1ab and ORF1a encodes 1ab and 1a polypeptide, respectively. ORF1ab gene is 21,291 nucleotides in length [44]. The order of other ORFs and genes downstream to the ORF1ab is: spike (S) gene (3,822 nt), ORF3a gene (828 nt), envelope (E) gene (228 nt), membrane (M) gene (669 nt) and nucleocapsid (N) (1260 nt) genes (Figure 3) [44].

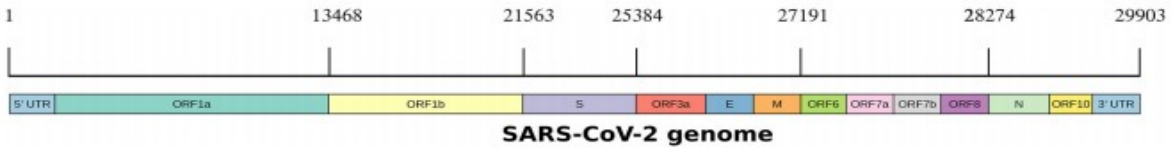

Figure 3. The SARS-CoV-2 genome is ~30Kb and consists of genes encoding structural and non-structural proteins. The structural proteins are nucleocapsid (N) protein, spike (S) protein, membrane (M) protein, and envelope (E) protein. Each box indicates a gene. The numbers on the axis indicate genome coordinates.

9. VARIANTS OF SARS-COV-2

Different genetic variants of SARS-CoV-2 have been emerging (Table 1). Most mutations are of little to no consequence, but sometimes, the virus acquires a mutation that gives it advantages over the other variants which may be associated with faster transmission and adverse illness.

9.1. Double mutant variant of SARS-CoV-2 in India

The double mutant variant or B.1.617 variant was first detected in October last year from Maharashtra, India. It represented 60% of the COVID-19 cases in Maharashtra [50,51]. This strain contains two important mutations: L452R and E484Q along with D614G mutations in spike protein [52]. Similarly, new variant of interest of SARS-CoV-2 called B.1.618 or triple mutant variant is seen from the West Bengal, India. This variant is highly transmissible with increased severity of disease and mortality. This strain carries following mutations: E484K, H146del, Y145del [52].

Table 1. Variants of SARS-CoV-2 and S gene mutations of concerns.

Name (Pango lineage)	Spike Protein Substitution	First Detected	Cause of Concern
B.1.1.7 (Alfa)	Spike: Δ69/70,Δ144 N501Y, D614G	United Kingdom	Immune escape. Diagnostic failure in assays targeting gene. Increased transmission.[47,48]
B.1.351 Beta	Spike: D80A, D215G, Δ241/242/243, K417N, N501Y, D614G	South Africa	~50% increased transmission. Significant decrease in susceptibility of antibodies.[42]
P1 Gama	Spike: L18F, T20N, P265, D138Y, N501Y, D614G, R190S, K417T, E484K, T1027I	Japan/ Brazil	Enhanced binding affinity to hACE2 receptor. Evade neutralizing Antibodies.[42]
B.1.617.2 Delta	D614G spike	India	It is 60% more transmissible than the Alfa variant. It has been detected in more than 130 countries
B.1.1.529 Omicron	Spike: Q493R, N501Y, S371L, S373P, S375F, Q498R and T478K	South Africa	Omicron variant had been confirmed in 149 countries. A significant growth advantage, higher secondary attack rates and a higher observed reproduction number compared to Delta
C.37 Lambda	Spike: L452R, D614G	United States (California)	~20% increased transmissibility. Reduced neutralization by convalescent and post vaccination sera.[42,49]
B.1.621 Mu	Mutated D614G spike	Columbia	The incidence of the Mu variant is approximately 0.1% globally. Mu variant possesses genetic changes or "mutations" that could make it more resistant to immunity from vaccines and previous infections

9.2. Omicron variant: a new variant of concern

On 24 November 2021, a new variant of concern was reported to WHO from South Africa. The Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE) has advised WHO to designate this variant as variant of concern (VOC), and the WHO has designated the B.1.1.529 (Omicron) variant as VOC [53]. Preliminary evidences suggest that latest Omicron variant have increased infectivity and pathogenicity [53]. This variant has number of mutations in receptor binding domain (RBD) that provide higher potential for transmission. The Q493R, N501Y, S371L, S373P, S375F, Q498R and T478K mutations provide significant binding affinity with human ACE2 [54]. The emergence of this heavily mutated variant and its quick spread around the world has again set off a global health alarm.

10. PREVENTION AND TREATMENT

Some preventive measures for COVID-19 are isolation of suspected patients, wearing face mask, proper and regular hand sanitization, steam inhalation, practice cough hygiene and making physical distancing from suspected patients. Treatment is supportive and symptomatic due to lack of effective anti-viral drugs against coronavirus. Antiviral drugs generally targeted the virus cycle like attachment, un-coating, replication of genetic material, translation and multiplication in the cell [33]. Different antiviral drugs such as oseltamivir, lopinavir and ribavirin have been used to reduce the viral loads [55]. Hydroxychloroquine and chloroquine drugs are also proposed to use for treatment of COVID-19. Remdisivir is also used to minimize viral load, [56] plasma therapy and coronavirus specific human monoclonal antibodies are also serving in the COVID-19 treatment [16,57]. A number of vaccines of various vaccine manufacturers such as Pfizer-BioNTech (RNA based), Moderna (RNA based), Johnson & Johnson's (viral vector based), Bharat Biotech (inactivated virus

based), Novavax (protein subunit based) are authorized and recommended for the prevention of COVID-19 [58].

11. CONCLUSION

The pandemic COVID-19 which started as an epidemic, epicentered in Wuhan, China at the end of the year 2019 has challenged the economy, medical and public health infrastructure of the entire world. This global health emergency has now been declared a pandemic by WHO. Now only time will tell what affect this pandemic will have on our lives. At the moment, there are number of supportive medicines and vaccines are available. Specific treatment for COVID-19 is matter of further research. The best strategies to deal with COVID-19 crisis include protection, prevention, controlling source of infection, maintaining proper hygiene and breaking off the mutated virus transmission. In this review an attempt has been made to compile the current findings about SARS-CoV-2 and COVID-19 variant. Further researches should be focused on improving the accuracy of early diagnosis for COVID-19, developing effective drugs and vaccines and efforts should be made to prevent further outbreaks of zoonotic origin.

Authors' Contributions: NVS suggested the concept, design and writing the first hand manuscript. HK did extensive literature search and correlate. VKS suggested the topic and provided the technical guide. All the authors read and approved the final manuscript. All the authors approved to the final version of the manuscript.

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REFERENCES

1. Singhal T. A review of coronavirus disease-2019 (COVID-19). Indian J Pediatrics. 2020; 87(4): 281-286.
2. He F, Deng Y, Li W. Coronavirus disease 2019: What we know? J Med Virol. 2020; 92(7): 719-725.
3. Andrews MA, Areekal B, Rajesh KR, Krishnan J, Suryakala R, Krishnan B, et al. First confirmed case of COVID-19 infection in India: A case report. Indian J Med Res. 2020; 151(5): 490.
4. Coronavirus (COVID-19) statistics. 2021. https://www.bing.com/search?q=corona+virus+(covid+19+)+statistics&cvid=059301049c18493f955bffc60588046e&aqs=edge.1.69i57j0j69i60l3j0l2.20956j0j1&pglt=299&FORM=ANNTA1&PC=U531. Accessed 29 April 2021.
5. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Bio Medica Atenei Parmensis. 2020; 91(1): 157.
6. Contini C, Di NM, Barp N, Bonazza A, De GR., Tognon M, Rubino S. The novel zoonotic COVID-19 pandemic: An expected global health concern. J Infect Develop Countr. 2020; 14(03): 254-264.
7. Weiss SR, Navas-Martin S. Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. Microbiol Mol Biol Rev. 2005; 69(4): 635-664.
8. Chan JFW, Lau SKP, Woo PCY. The emerging novel Middle East respiratory syndrome coronavirus: the “knowns” and “unknowns”. J Formosan Med Assoc. 2013; 112(7): 372-381.
9. Zhou P, Yang XL, Wang XG, Hu B, Zhang, L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020; 579(7798): 270-273.
10. Chan-Yeung, M, Xu RH. SARS: epidemiology. Respirology. 2003; 8: S9-S14.
11. Gretebeck LM, Subbarao K. Animal models for SARS and MERS coronaviruses. Curr Opin Virol. 2015; 13: 123-129.
12. Schoeman D, Fielding BC. Coronavirus envelope protein: current knowledge. Virol J. 2019; 16(1): 1-22.

13. Kirchdoerfer RN, Cottrell CA, Wang NP J, Yassine HM, Turner HL, et al. Pre-fusion structure of a human coronavirus spike protein. Nature. 2016; 531(7592): 118-121.
14. Gupta MK, Vemula S, Donde R, Gouda G, Behera L, Vadde R. In-silico approaches to detect inhibitors of the human severe acute respiratory syndrome coronavirus envelope protein ion channel. J Biomol Struct Dynam. 2020: 1-11.
15. Lissenberg A, Vrolijk MM, Van Vliet ALW, Langereis MA, de Groot-Mijnes JDF, Rottier PJM, De Groot RJ. Luxury at a cost? Recombinant mouse hepatitis viruses expressing the accessory hemagglutinin esterase protein display reduced fitness in vitro. J Virol. 2005; 79(24): 15054-15063.
16. Boopathi S, Poma AB, Kolandaivel P. Novel 2019 coronavirus structure, mechanism of action, antiviral drug promises and rule out against its treatment. J Biomol Struct Dynam. 2020: 1-10.
17. Kaushik H, Singh VK. Mathematics of Covid-19 in India and their possible control by *Allium sativum* (l.). Asian J Adv Med Sci. 2020: 21-27.
18. Cheng ZJ, Shan J. Novel coronavirus: where we are and what we know. Infection. 2019; 48(2): 155-163.
19. He Y, Zhou Y, Liu S, Kou Z, Li W, Farzan M, Jiang S. Receptor-binding domain of SARS-CoV spike protein induces highly potent neutralizing antibodies: implication for developing subunit vaccine. Biochem Biophys Res Commun. 2004; 324(2): 773-781.
20. Du L, Zhao G, He Y, Guo Y, Zheng BJ, Jiang S, Zhou Y. Receptor-binding domain of SARS-CoV spike protein induces long-term protective immunity in an animal model. Vaccine. 2007; 25(15): 2832-2838.
21. Li W, MooreMJ, Vasilieva N, Sui J, Wong SK, Berne MA, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature. 2003; 426(6965): 450-454.
22. Kuba K, Imai Y, Rao S, Gao H, Guo F, Guan B, et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus–induced lung injury. Nature Med. 2005; 11(8): 875-879.
23. Wang S, Guo F, Liu K, Wang H, Rao S, Yang P, Jiang C. Endocytosis of the receptor-binding domain of SARS-CoV spike protein together with virus receptor ACE2. Virus Res. 2008; 136(1-2): 8-15.
24. Aoe, T. Pathological Aspects of COVID-19 as a Conformational Disease and the Use of Pharmacological Chaperones as a Potential Therapeutic Strategy. Front Pharmacol. 2020; 11: 1095.
25. Rahman N, Basharat Z, Yousuf M, Castaldo G, Rastrelli L, Khan H. Virtual screening of natural products against type II transmembrane serine protease (TMPRSS2), the priming agent of Coronavirus 2 (SARS-CoV-2). Molecules. 2020; 25(10): 2271.
26. Huang Y, Yang C, Xu XF, Xu W, Liu SW. Structural and functional properties of SARS-CoV-2 spike protein: Potential antivirus drug development for COVID-19. Acta Pharmacol Sin. 2020; 41: 1141-1149.
27. Yadav R, Chaudhary JK, Jain N, Chaudhary PK, Khanra S, Dhamija P, et al. Role of Structural and Non-Structural Proteins and Therapeutic Targets of SARS-CoV-2 for COVID-19. Cells. 2021; 10: 821.
28. Shang J, Wan Y, Luo C, Ye G, Geng Q, Auerbach A, Li F. Cell entry mechanisms of SARS-CoV-2. Proc Nat Acad Sci. 2020; 117(21): 11727-11734.
29. Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GV, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol. 2004; 203(2): 631-637.
30. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New Engl J Med. 2020; 382: 1199-1207.
31. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020; 323(13): 1239-1242.

32. Linton NM, Kobayashi T, Yang Y, Hayashi K, Akhmetzhanov AR, Jung SM, et al. Incubation period and other epidemiological characteristics of 2019 novel coronavirus infections with right truncation: a statistical analysis of publicly available case data. J Clin Med. 2020; 9(2): 538.
33. Kaushik H, Singh VK. Novel Coronavirus (SARS-CoV-2): A Pandemic Era. Coronavirus Disease (Covid-19): Scoping Review, Chapter 7. 2020: 110-127. https://www.kdpublications.in.
34. Kabir MA, Ahmed R, Iqbal SMA, Chowdhury R, Paulmurugan R, Demirci U, Asghar W. Diagnosis for COVID-19: current status and future prospects. Expert Rev Mol Diagn. 2021: 1-20.
35. Dai WC, Zhang HW, Yu J, Xu HJ, Chen H, Luo SP, et al. CT imaging and differential diagnosis of COVID-19. Can Assoc Radiologists J. 2020; 71(2): 195-200.
36. Chan JFW, Yuan S, Kok KH, To KKW, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020; 395(10223): 514-523.
37. Loon SC, Teoh SCB, Oon LLE, Se-Thoe SY, Ling AE, Leo YS, Leong, H. N. The severe acute respiratory syndrome coronavirus in tears. Brit J Ophthalmol. 2004; 88(7): 861-863.
38. Wilson NM, Norton A, Young FP, Collins DW. Airborne transmission of severe acute respiratory syndrome coronavirus-2 to healthcare workers: a narrative review. Anaesthesia. 2020; 75(8): 1086-1095.
39. Lewis D. Is the coronavirus airborne? Experts can't agree. Nature. 2020; 580(7802): 175.
40. Lai MY, Cheng PK, Lim WW. Survival of severe acute respiratory syndrome coronavirus. Clin Infect Dis. 2005; 41(7): e67-e71.
41. World Health Organization. Genomic sequencing of SARS-CoV-2 A guide to implementation for maximum impact on public health, 8 January 2021. https://apps.who.int/iris/bitstream/handle/10665/338480/9789240018440-eng.pdf?sequence=1&isAllowed=y. Accessed: 15 May 2021.
42. Bhardwaj R, Agrawal A. How coronavirus survives for days on surfaces. Physics Fluids. 2020; 32(11): 111706.
43. Srivastava S, Banu S, Singh P, Sowpati DT, Mishra RK. SARS-CoV-2 genomics: An Indian perspective on sequencing viral variants. J Biosci. 2021; 46(1): 1-14.
44. Sah R, Rodriguez-Morales AJ, Jha R, Chu DK, Gu H, Peiris M, et al. Complete genome sequence of a 2019 novel coronavirus (SARS-CoV-2) strain isolated in Nepal. Microbiol Resour Announc. 2020; 9(11): e00169-20.
45. Wang Y, Mao JM, Wang GD, Luo ZP, Yang L, Yao Q, Chen KP. Human SARS-CoV-2 has evolved to reduce CG dinucleotide in its open reading frames. Sci Reports. 2020; 10(1): 1-10.
46. Srinivasan S, Cui H, Gao Z, Liu M, Lu S, Mkandawire W, et al. Structural genomics of SARS-CoV-2 indicates evolutionary conserved functional regions of viral proteins. Viruses. 2020; 12(4): 360.
47. Davies NG, Abbott S, Barnard RC, Jarvis CI, Kucharski AJ, Munday JD, et al. Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. Science. 2021; 372(6538): eabg3055.
48. Emary KR, Golubchik T, Aley PK, Ariani CV, Angus B, Bibi, S, et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. Lancet. 2021; 397(10282): 1351-1362.
49. Deng X, Garcia-Knight MA, Khalid MM, Servellita V, Wang C, Morris MK, et al. Transmission, infectivity, and antibody neutralization of an emerging SARS-CoV-2 variant in California carrying a L452R spike protein mutation. MedRxiv. 2021.
50. Yadav P, Sapkal GN, Abraham P, Ella R, Deshpande G, Patil DY, et al. Neutralization of variant under investigation B. 1.617 with sera of BBV152 vaccinees. BioRxiv. 2021.

51. Talukdar S. Mutant Variants of Coronavirus in India: What we Know So Far. 12 May 2021. https://www.newsclick.in/mutant-variants-coronavirus-india-what-we-know-far. Accessed 20 May 2021.
52. Sahoo JP, Mishra AP, Samal KC. Triple Mutant Bengal Strain (B. 1.618) of Coronavirus and the Worst COVID Outbreak in India. Biotica Res Today. 2021; B(4): 261-265.
53. World Health Organization. Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern. https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern. Accessed 16 December 2021.
54. Kumar S, Thambiraja T S, Karuppanan K, Subramaniam G. Omicron and Delta Variant of SARS-CoV-2: A Comparative Computational Study of Spike protein. bioRxiv. 2021.
55. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395(10223): 497-506.
56. Sinha N, Balayla G. Hydroxychloroquine and covid-19. Postgrad Med J. 2020; 96(1139): 550-555.
57. Koenig KL. Identify-isolate-inform: a modified tool for initial detection and management of Middle East Respiratory Syndrome patients in the emergency department. Western J Emerg Med. 2015; 16(5): 619.
58. Centre for disease control and prevention. Different COVID-19 Vaccines: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines.html. Accessed 2 May 2021.