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SARS-CoV-2, the COVID-19 virus and its pandemic in India

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Abstract: *COVID-19 a new pandemic is now a global crisis with virus infection as acute respiratory syndrome. The virus SARS-CoV-2 belonging to Coronaviridae was first reported from Wuhan city, Hubei province of China and thereafter WHO declared COVID-19 pandemic. The virus reported to be originated in bats and was transmitted to humans through an unknown intermediary animal in Wuhan, Hubei province, China in December 2019.The first case from India was reported from Kerala also, traced to originate from China. The virus detected from bats might have migrated to some animals and eventually attacked humans. Later, SARS-CoV-2 is found infecting humans without any animal intermediary. The infection is mild to moderate is diagnosed to cause severe respiratory problems and death in cases of severity depending on other critical illness of the patient. In case of severity, clinical support with certain therapeutics is being done to save the life. Physical distancing measures and movement restrictions with lockdowns were imposed to slow down the COVID-19 transmission by breaking the chain. Some variants have been traced in countries where virus spread is severe. Several successful trials were made to develop vaccine against the virus. COVID-19 Herd immunity threshold (HIT) estimates from mathematical models are as high as 60 to 80 percent making vaccination as an important criterion in checking virus infection.*

Keywords: *SARS-CoV-2,COVID-19, diagnosis, therapeutics, vaccines, Herd immunity*

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I. Introduction

National authorities in China reported to WHO on December 31, 2019 about cases of pneumonia with unknown aetiology. Wuhan city, Hubei province of China from December 31, 2019 to January 3, 2020, witnessed a total of 44 cases with pneumonia of unknown aetiology[1]. The Director-General declared the novel *coronavirus* outbreak (2019-nCoV) a Public Health Emergency of International Concern (PHEIC) on 30th January 2020[2] . Sooner 25 other countries have reported COVID-19 outbreak with 794 cases and three deaths, while China had 70,635 confirmed cases with 1,772 deaths[3].The cases initially identified had a history of exposure to the Huanan Seafood Wholesale Market[4]. It is now confirmed that this *coronavirus*, SARS-CoV-2, might have originated in bat and entered to another animal, possibly the pangolin, which then passed it on to humans. Later the spread between people without any animal intermediary became a pandemic with many countries across the globe reporting cases of *coronavirus*, SARS-CoV-2. *Coronavirus* (CoV) belong to a large family of enveloped RNA viruses of both medical and veterinary importance. This group is known to cause the common cold to more severe diseases such as Middle East respiratory syndrome (MERS)-CoV and severe acute respiratory syndrome (SARS)-CoV.

II. Materials And Methods

The paper is based on the review made on the research made on the virus and information available on electronic media and published research. A detailed review was made to brief information on the *coronovirus*, its pandemic in Indian context, events related to development of vaccine against the virus and chance for herd immunity in the country. The paper summarises various variants that have evolved due to spread in large communities throughout the world.

III. Results And Discussion

COVID-19 disease is an infectious disease that causes severe respiratory illness with most patients developing mild to moderate symptoms. Dry cough, fever, fatigue, headache, body ache, sore throat, olfactory loss of smell and taste, nausea and vomiting are some of the most common symptoms in patients infected with the virus. The severity of symptoms may vary with the immunity levels and in cases with chronic health problems like diabetes, asthma, high blood pressure, heart disease, liver or kidney disease, obesity, cancer, etc. Repots confirmed that hypertension (56.8%), diabetes (31.2%) and coronary heart diseases (21.5%) were the most common morbities in COVID-19 mortality[5].

3.1. Genetics of corona viruses: *Coronaviruses* are enveloped RNA viruses distributed widely among mammals and birds. Spike like projections on its surface give them a crown like appearance and hence the name *coronavirus* was suggested[6]. They cause respiratory diseases and in some cases neurologic illness or hepatitis[7]. These viruses infect their hosts in a species-specific manner with acute infections. Infections are transmitted via respiratory and fecal-oral routes. *Coronaviruses* have the largest genomes among all RNA, a distinct feature of these group viruses. This group employ a complex mode of gene expression to assemble progeny virions, a pathway unique among enveloped RNA viruses. *Coronaviruses* are classified under the family *Coronaviridae* along with *toroviruses*[8]. Corona viruses are roughly spherical with an average diameter of 80-120nm. There are three protein components of the viral envelope called Spike Protein (S) prominently S glycoprotein (formerly called E2)[9]. This protein mediates receptor attachment and viral and host cell membrane fusion[10]. The Member glycoprotein, formerly called E1 is the abundant constituent of coronaviruses[11,12] to give the virion envelope a shape. Envelope Protein (E) formerly called sM is a small polypeptide of 8.4 to 12 kDa (76–109 amino acids), that is only a minor constituent of virions. Nucleocapsid Protein (N) which ranges from 43 to 50 kDa, is the helical nucleocapsid to bind the genomic RNA in a beads-on-a-string fashion[13]. *Coronavirus* genomes are extremely large, nonsegmented, single-stranded RNA molecules of positive sense, that is, the same sense as mRNA[14-17].The coronavirus accessory genes were group 2 HE protein, the I protein and the SARS-CoV 3a protein, have been shown to be components of virions[18]. Accessory genes were group-specific genes, but with diversity as revealed by recently discovered *coronaviruses*.

3.2. Pandemic in India: First case of COVID-19 infection reported in Government Medical College, Thrissur, Kerala on January 31, 2020 with a 20year old lady having travel history of Wuhan city, China, on January 23, 2020. The initial swabs remained positive till day 17 after which the patient was discharged on February 20, 2020 with later swab tests being negative[19]. Slowly the virus spread across the country causing severe disease and mortality. The disease spread across the society and all age groups. In India COVID 19 has recorded a total of 28,175,044 cases as on June 2021 including first wave of the epidemic with cumulative deaths of 3,51,309 There is a marginal difference in the age group with severity cases of aged persons. First wave experienced cases with higher proportion with sore throat, cough, while second wave reported more cases of breathlessness compared to first wave period.

3.3. Diagnosis of COVID-19 infection: It is necessary to clinically examine a patient whether he is positive or negative to the virus and seriousness of infection before giving any medication. Virus diagnosis is by specific molecular tests on respiratory samples (throat swab/ nasopharyngeal swab/ sputum/ endotracheal aspirates). Virus may also be detected in the stool and in severe cases blood samples were also drawn[20]. As per current clinical diagnosis, transplacental transmission from pregnant women to their foetus has not been described[21]. In India different types of tests are available to identify and to detect COVID-19 infection in rapid and efficient manner. Some of the most commonly used tests used are Molecular tests, COVID-19 antigen test and COVID-19 antibody test. A). Molecular test or RT-PCR (reverse transcription-polymerase chain reaction) test is a method to detect Virus genetic material by converting RNA to DNA by reverse transcriptase. This test is also known as nucleic acid amplification test (NAAT). A nasal or throat swab sample is taken to detect the virus. RT-PCR can detect the virus in asymptomatic persons. However, this test cannot detect previous infection if any. Only NABL (National Accreditation Board for Testing and Calibration Laboratories) accredited laboratories approved by ICMR are permitted to handle the COVID-19 samples owing to contagious nature of the virus. B). COVID-19 Antigen Tests: This is a rapid diagnostic test faster than molecular test detecting COVID-19 virus antigen which triggers an immune response. This test helps to detect active *coronavirus* in the sample. C). COVID-19 Antibody Test: This is a serology test to detect COVID-19 antibodies in blood sample developed in response to COVID-19 infection. This test is only about immune response but not detects any active infection. It is tested by drawing blood sample. Antibody test is only for surveillance purposes, and can determine if a patient has previous infection of *coronavirus.* D).TruNat test: A test to by detecting RdRp enzyme found in the virus RNA. TrueNat machine is a portable machine which runs on battery. It detects the virus in nasal or oral swabs. E).CT scan: In abnormal cases where patients had no positive molecular test CT scans have been used to diagnose COVID-19. It is also abnormal in asymptomatic patients/ patients with no clinical evidence of lower respiratory tract involvement[22].

3.4. Therapeutic management of COVID-19 patients: Detailed guidelines for critical care management for COVID-19 have been directed by the WHO. As of now there is, no approved treatment for COVID-19[23]. Certain antiviral drugs are being used based on the experience with SARS and MERS. Treatment to patients vary with symptoms and severity of infection stage procedures as lay down by ICMR, Govt. of India in its clinical guidance of adult COVID-19 patients on protocol drugs to be administered (ICMR)[24] bsed on symptoms of the patient. Remdesivir, an antiviral drug currently recommended for use in hospitalized patients who require supplemental oxygen. Clinical trials showed that Remdesivir as effective and shorten recovery time but does not reduce mortality[25-28]. Trials with steroid Dexamethasone showed good response with reduced

mortality in severe Covid-19 infection who need oxygen therapy or are on ventilators[29,30]. Favipiravir is another oral antiviral drug, received Emergency Use Authorisation (EUA) for treatment of mild or moderate infections. Clinical trial data in China showed a decrease in viral load. Tocilizumab works when the immune response is already inflamed and helps to arrest the impending cytokine storm, which affects other organ functions. The treatment is supported to counter any other infections with antibiotics, Azithromycin and Ivermectin. Recently the Drug Controller General of India (DCGI) approved a drug called 2-deoxy-d-glucose (2-DG) a modified glucose molecule works as anti-viral agent use among patients with moderate and severe COVID-19. This drug was jointly developed by the Institute of Nuclear Medicine and Allied Sciences (DRDO), and Dr Reddy's Laboratories, Hyderabad. ICMR, New Delhi is monitoring the treatment process and giving directions on retention and discontinuation of certain drugs in COVID-19 infection.

3.5. Convalescent Plasma Therapy: CP therapy works better when infused early on in the treatment cycle. Immunological studies have reported diverse antibodies in the serum of recently recovered patients from virus infections. These antibodies bind the receptor-binding site of viral spike protein (S-RBD) and inhibit the virus amplification. CP contains factors like, polyclonal antibodies against the target agent capable of providing immunity. However, due to insufficient data on the efficacy and effectiveness of CP therapy in COVID-19 ICMR has prescribed direction on its use.

3.6. Variants of SARA-CoV-2: When a virus circulates in a population is likely to mutate and undergoes changes to evolve as variant. Genetic variants of SARS-CoV-2 have been emerging around the world. Viral mutations and variants are being routinely monitored through sequence-based surveillance, laboratory studies, and epidemiological investigations. ECDC regularly monitors variants based genomic screening performed using an open source algorithm[31].The mutation rate of single stranded RNA viruses is observed to be more compared to DNA stranded. SARA-CoV-2 is reported mutate and variants have one specific mutation, D614G which is makes to spread faster[32]. The genome is reported to be of 27-31kb in length increasing number of mutations. The first mutation was found in the China in the initial stages of the pandemic[33]. There is evidence that variants with this mutation spread more quickly than viruses without this mutation[34]. The weekly ECDC variant surveillance data report can be found in the weekly COVID-19 country overviews published on ECDC's website[35]. Based on evidence concerning Transmissibility, Immunity, Infection severity three categories, viz., variant of concern (VOC), variant of interest (VOI), or variant under monitoring are made. *Coronavirus* variants are named after letters of the Greek alphabet instead of their place of first discovery, as per the directions of WHO[36]. Based on certain attributes like potential reduction in neutralization by some EUA monoclonal antibody treatments[37,38] and reduced neutralization by post-vaccination sera[39,40] a few variants have been described **(Table 1)**.

Table 1: Variants of concern (VOC) and Variants of interest (VOI)[a-d]

Variants of concern (VOC)					Variants of interest (VOI)				
WHO label	Lineage + additional mutations	Country first detected	Spike mutations of interest	Year and month of detection	WHO label	Lineage + additional mutations	Country first detected	Spike mutations of interest	Year and month of detection
Alpha	B.1.1.7	United Kingdom	N501Y, D614G, P681H	September 2020	Eta	B.1.525	Nigeria	E484K, D614G, Q677H	December 2020
	B.1.1.7 +E484K	United Kingdom	E484K, N501Y, D614G, P681H	December 2020	Epsilon	B.1.427/ B.1.429	USA	L452R, D614G	September 2020
Beta	B.1.351	South Africa	K417N, E484K, N501Y, D614G, A701V	September 2020	Theta	P.3	The Philippines	E484K, N501Y, D614G, P681H	January 2021
Gamma	P.1	Brazil	K417T, E484K, N501Y, D614G, H655Y	December 2020		B.1.616	France	V483A, D614G, H655Y, G669S	February 2021
Delta	B.1.617.2	India	L452R, T478K, D614G, P681R	December 2020	Kappa	B.1.617.1	India	L452R, E484Q, D614G, P681R	December 2020

[a] SARS-CoV-2 variants of concern as of 3 June 2021 - ECDC https://www.ecdc.europa.eu › covid-19 › variants-concern [b]WHO Updates the Nomenclature of SARS-CoV-2 Variants . https://www.the-scientist.com › news-opinion › who [c]Wu K, A.P. Werner, J.I.Moliva, et al. 2021. mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants. BioRxiv 2021. doi: https://doi.org/10.1101/2021.01.25.427948external icon [d]Garcia-Beltran, W, E.C. Lam, K. St. Denis, et al. Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity Cell 2021. doi: https://doi.org/10.1016/j.cell.2021.03.013external icon	B.1.620	Unclear	S477N, E484K, D614G, P681H	February 2021
	B.1.621	Colombia	R346K, E484K, N501Y, D614G, P681H	January 2021

3.7. Vaccine development against COVID-19: Vaccines allow the body to build immunity by activating Thymus and Bone marrow lymphocytes, cells that, respectively, recognize the targeted virus and produce antibodies to combat it. Generally vaccine contains only a fraction of virus and never causes disease. However, persons may experience certain side effects after vaccination like, a fever, fatigue, headaches, body aches, nausea, pain and itchy rash which subside with time. Polyethylene glycol (PEG), in mRNA vaccines might cause allergic reactions. Anaphylaxis, an extremely rare side effect of vaccination involves low blood pressure, nausea, and difficulty breathing. Reproductive hormones, estrogens and testosterone, may vary in immune response and estrogens may deliver more antibodies, leading to a higher immune response [41]. Around 15 vaccines have been developed around the world and currently being administered **(Table 2)**.

Table 2: Vaccines developed and being used in at least two countries

S.N	Name	Type of vaccine	% Efficacy rate
1	BNT162b2 (Comirnaty) (Pfizer-BioNTech)	mRNA	95
2	mRNA-1273 (Moderna)	mRNA	94.5
3	Ad26.COV2.S Janssen (Johnson & Johnson)	Viral vector	66
4	AZD1222 (Vaxzevria) (Oxford-AstraZeneca)	Viral vector	81.3
5	Covishield* (Serum Institute of India)	Viral vector	81.3
6	Ad5-nCov (CanSino)	Viral vector	65.3
7	Sputnik V (Gamaleya)	Viral vector	91.6
8	Covaxin (Bharat Biotech)	Inactivated	80.6
9	BBIBP-CorV (Sinopharm) (Beijing)	Inactivated	79.3
10	Inactivated (Vero Cell) (Sinopharm) (Wuhan)	Inactivated	72.5
11	CoronaVac (Sinovac)	Inactivated	50.4
12	CoviVac (KoviVac) (Chumakov Center)	Inactivated	Unknown
13	QazCovid-in (QazVac) (Kazakhstan RIBSP)	Inactivated	Unknown
14	RBD-dimer Anhui Zhifei (Longcom)	Protein subunit	Unknown
15	EpiVacCorona (FBRI)	Protein subunit	Unknown

3.8. Vaccines in India: Three vaccines have been registered and recommended for COVID-19 infection in India. Covishield vaccine has been developed using the viral-vector platform technology. A chimpanzee adenovirus – ChAdOx1 – has been modified to mimic as COVID-19 spike protein in the cells of humans preparing an immunity mechanism against SARA-CoV-2 [42,43]. Covaxin-code named BBV152 is developed by Bharat Biotech in collaboration with the Indian Council of Medical Research ICMR). Covaxin an Indian vaccine developed through a traditional methodology by augmenting the SARA-CoV-2 sample through vero cells and deactivating with beta-propiolactone which binds to genome leaving viral particle intact. This deactivated virus is mixed with aluminium based adjuvant for use as vaccine. The interval between the 2 doses is 4-6 weeks . Both Covaxin and Covishield are intramuscular vaccines. The interval between 1st and 2nd doses of Covishield is 12-16 weeks. The Serum Institute (SII), the Indian maker of the vaccine, says Covishield is "highly effective" and backed by phase III trial data from Brazil and United Kingdom[44]. The effectiveness of the Covishield vaccine is nearly 90% as per the global reports and Covaxin's 81% according to interim 3rd phase trial results[45]. Sputnik V (Gam-COVID-Vac) is an adenoviral-based, two-part vaccine developed by the Russian scientists and registered in India. The vaccine is developed by inserting Virus spike protein, S-proteininto a familiar adenovirus vector for delivery into a human cell. To ensure lasting immunity, Sputnik Vuses two different types of adenovirus vectors (rAd26 and rAd5) for the first and second vaccination[46].

3.9: Herd immunity: Herd immunity also, known as community immunity protects against communicable infections. Herd immunity is acquired when most of a population becomes immune to an infectious disease, thus preventing the spread of the disease. Herd immunity is achieved under condition of population vaccinated and larger population developed immunity in response to virus infection. In general about 70% to 90% of a population has to attain immunity for community immunity. COVID-19 Herd immunity threshold (HIT) estimates from mathematical models are as high as 60 to 80 percent making vaccination drive an important

criterion in checking virus infection [47-50].Herd immunity helps vulnerable groups by breaking chain transmission. Physical distancing measures and movement restrictions with lockdowns laid down to slow down the COVID-19 transmission. Studies have confirmed production of different T cell subsets and B cells in response to viral spike proteins, as a part of adaptive immunity against SARS-CoV-2. Cross-reactive T-cells have also, been recorded in patients who have been previously exposed to coronaviruses.

IV. Conclusion

Infectious diseases of this kind pandemic nature are to be managed through vaccination and prevention of spread by breaking infection chain. As on 12 June 24.4Cr doses were given of which 4.63Cr were fully vaccinated (3.4%) in India as against 43.3 and 43.8% of full vaccination in USA and UK .Serious efforts to vaccinate people help reducing hospitalizations and deaths from COVID-19, even before attaining herd immunity. Presence of a large number of asymptomatic or mild cases, a low infection-fatality ratio in the COVID-19 situation in India suggests theory of both cross-immunity and herd immunity among the population. The disease might not disappear completely soon, but its importance is likely to reduce with time with community immunity.

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