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COVID-19: CURRENT PERSPECTIVES ON VACCINES AND CLINICAL MANAGEMENT

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ABSTRACT

The global pandemic Corona Virus Disease-2019 (COVID-19) is being transmitted aggressively in forms of progressive waves even after the 1.5 years of its occurrence. Development of vaccine has nearly concluded the prevention of mortality in suffered patients. Along with vaccination, the prevention of further transmission is aimed by several countries with the help of social distancing, bearing a mask and appropriate sanitization. In absence of any specific treatment, this study was needed to compile the available research in relation to transmission, etiology, pathophysiology, and the available options to clinically manage the patients suffering from COVID-19.

Newly identified β -coronavirus has genomic similarities with SARS-CoV and MERS-CoV. Such similarity made basis for new virus to be known as SARS-Corona virus-2 (SARS-CoV-2). A total of 40,12,863 people globally amongst 18,32,34,647 infected population have lost their life till 20th June 2021. The prime mechanism of transmission was alleged to be animal to human transmission. Thereafter, consequent cases were not related with such transmission concluding human to human exposure. CDC (Disease Control and Prevention) investigated the first case of Wuhan and interpreted that incubation period could range generally from three to seven days and lasts until 2 weeks and the lengthiest time from contamination to symptoms was found to be 12.5 days. The virus bears crown like glycoprotein's spike on its envelop and hence it is termed corona from *coronam* (Latin) meaning crown in English. There is no treatment available currently for COVID-19 either in form of vaccine or in form of antiviral drug. The symptomatic relief is only the option to deal with the disease. Oxygen therapy remains the major intervention for severe patients. Convalescent plasma or immunoglobulins were used to enhance the rate of survival in SARS patients. Chloroquine, Ruxolitinib, Baricitinib and fedratinib claimed to lower the symptoms in associate pneumonia. A very few patients have been enrolled in clinical trials. No scientific evidence so far exists to support the chance of vertical transmission of COVID-19 contamination from the pregnant mother to the baby. Sustaining staff mental well-being is crucial to better control infections, even though the best approach to combat with this through the epidemic time remains blurred. Vaccines seem to be most promising solution to attenuate newer strains of corona virus. The recognition of genomic sequence as well study of protein structure of corona virus-2019, were studied in very lesser time. This allowed the development of inactivated or live attenuated vaccine for the prevention of COVID-19.

Keywords: COVID-19, Vaccine, Pandemic, Transmission, Clinical management.

1. INTRODUCTION

The outbreak of Pandemic COVID-19 is destructing the world [1] Humans are helpless even with the revolutionary technologies in all dimensions of life. Corona virus target human respiratory system primarily causes Severe-Acute Respiratory Syndrome (SARS-CoV) & Middle-East Respiratory Syndrome (MERS-CoV) [2]. Disease originated with the reporting of cluster of pneumonia cases triggered by a newly recognized β -coronavirus in the Chinese city Wuhan [3]. β -coronavirus confirmed to infect humans, is

seventh corona virus with genomic similarity of about 70-80% to SARS-CoV, 50% to MERS-CoV and 96% to that of bat corona virus. β -coronavirus uses similar angiotensin-converting enzyme II (ACE2) cell receptor as by SARS-CoV [4-6].

Word Health Organization (WHO) on 12 Januray 2020 initially named this corona virus as 2019-novel coronavirus (2019-nCoV) and subsequently on 11 February 2020 the disease caused by this novel corona virus was named to be coronavirus disease 2019 (COVID-19) [7]. The outburst of COVID-19 could not limit within the China rather it started spreading aggressively worldwide through human to human transmission. WHO has already assessed the alarm levels of spread, severity & inaction and characterized the COVID-19 as global pandemic in its situation report-51 on 11 March 2020 [8].

2. TRANSMISSION

The very first case of COVID-19 was interlinked with animal to human transmission from the seafood's wholesale market of Wuhan in China. The prime mode of spread was alleged to be animal to human transmission. Thereafter, successive cases were not connected with such transmission concluding human to human exposure. Peoples having the symptoms of corona virus infection are most vulnerable source of spreading COVID-19. Additionally, the person without symptoms also transmits the disease. The study suggests isolation to be the most prominent mechanism for breaking the outbreak of this pandemic [9]. WHO guided that quarantine, social distancing, and isolation of infected populations can prevent the transmission of the pandemic [10].

As in the case of other viral respiratory syndromes, the spread is supposed to arise through the droplets released from sneezing & coughing. In many studies, transmission of SARS-CoV-2 in China indicated the transmission through close contact with infected individual. Chinese Center for CDC (Disease Control and Prevention) investigated the first case in Wuhan and interpreted that incubation period could range generally from three to seven days and lasts till two weeks and the longest period from getting infected to the appearance of symptoms was found to be 12.5 days. The study also revealed that virus replicated to double about every seven days [11]. Extended viral shedding offers the basis for an approach of isolation of affected patients and optimum antiviral interventions in coming days [12]. Above mechanisms of transmission is on the basis of initial studies only. Therefore, it is emphasized the need of further studies with respect to incubation & transmission.

3. ETIOLOGY

The virus bears crown like glycoprotein's spike on its envelop and hence it is termed corona from *coronam* (Latin) meaning crown in English. It is positive stranded RNA virus belonging to subfamily: *Orthocoronavirinae* of the *Coronaviridae* family (order *Nidovirales*). It is classified into 4 species of corona virus viz. Alphacoronavirus $(\alpha$ -CoV), Betacoronavirus (β -CoV), Deltacoronavirus $(\delta$ -CoV) & Gammacoronavirus (γ -CoV) [13]. Betacorona-virus (β -CoV) further, subdivided into 5 subgenera [14]. Characterization of genome has already shown the probability of α -CoV and β -CoV in bats and rodents. On the other hand, δ -CoV and γ -CoV are represented by some avian species [9]. Hepatic, enteric, respiratory, and neurological diseases are originated through these large families of viruses in diverse species including camels, cats, cattle & bats. Overall, evaluations advocate that 2% of the global populace is vigorous carriers of corona virus whereas the family of these viruses is responsible to cause acute breathing obstructions in 5% to 10% population. It was identified that 89% nucleotide identity of genome with bat SARS like corona virus (CoVZXC21) and 82% with that of human's SARS corona virus in cluster patient of atypical pneumonia visited in Wuhan, China [15]. Such similarity made basis for new virus to be known as SARS-Corona virus-2 (SARS-CoV-2).

4. PATHOPHYSIOLOGY

Corona virus is enveloped positive stranded RNA having nucleocapsid in their structure. Viral structure and genome studies are important considerations to know the underlined pathogenesis [16]. Corona virus's genomic structure is recognized as a largest RNA virus with 3'-poly-A tail and a 5'-cap structure of 30 kb in length (approx.) Synthesis of polyprotein pp1a and polyprotein pp1ab is identified from viral RNA [9]. The transcription functions through the replicationtranscription complex (RCT) sorted out in bifold film vesicles and by means of the combination of subgenomic RNAs (sgRNAs) arrangements. Notably, transcription ends at transcription organizational successions, situated amid the open reading frames (ORFs) that functions as template for the construction of subgenomic-mRNAs. In an atypical corona virus genome, in any occasion 6 ORFs can be available. Amongst these, a frameshift anywhere in the range of ORF-1a and ORF-1b guides the construction of both pp-1a and pp-1ab polypeptides that are managed by virally encoded chymotrypsinlike protease (3CL-pro) or principle protease (M-pro), just as a couple of papain like proteases for delivering 16 non-structural proteins (nsps). Separately, from ORF-1a and ORF-1b, different ORFs encode for auxiliary proteins, together with spike, layer, envelope, nucleocapsid proteins & accessory proteic chains [17]. Pathophysiology as well as mechanisms of virulence for CoVs, and consequently also of SARS-CoV-2 have

associations to the function of the nsps and organizational proteins. Such as, research emphasized that nsp can block the host's native immunity [18]. Amid functions of these structural proteins, the envelope plays critical role in pathogenicity of virus as it encourages assembly of virus and release. Nevertheless, several of these features (for example, those of nsp2 & 11) have not described till now. SARS-CoV-2 is assumed to distress the host cells via ACE2 and cause damage to the myocardial cells. But definite mechanism lying behind such damage is not clearly known. Therefore, special care for cardiovascular patients while treating COVID-19 is of great importance [16]. Another study warns about the consequent treatment of hypertension & diabetes with ACE-2 provoking drug substances increases the risk of developing severe and fatal COVID-19 [19].

Research will be expected to establish the basic structural facet of SARS-COV-2 underlying the pathogenetic events. Contrasted with SARS, for instance, preliminary clinical studies show less extra respiratory correlations, although because of the absence of broad information, it is impossible to reach at a definite clinical conclusion.

5. CLINICAL MANAGEMENT

Existing management for COVID-19 is limited to the supportive therapies while principal cause of mortality is the acute respiratory distress syndrome (ARDS) resulting in respiratory failure [20]. There is no treatment available currently for COVID-19 in form of any antiviral drug. The symptomatic relief is only the option to deal with the disease. Oxygen therapy remains the major intervention for severe patients. Mechanical ventilation & hemodynamic support may be necessary to avoid respiratory failure due to oxygen therapy and managing septic shock respectively.

Several COVID-19 infected patients showed only mild flu like symptoms and recovered quickly [21]. Abnormalities in CT imaging of COVID-19 resulting pneumonia patient even in without symptoms show quick progression from focal unilateral to diffuse bilateral ground glass opacities progressed or co-existed with unions within 1 to 3 weeks. The imaging features along with clinical and laboratory findings may facilitate an early diagnosis [22]. On 13 March 2020, WHO released a document summarizing the clinical management of severe-acute respiratory contamination on the suspicious occurrence of covid-19 disease. The guidelines presented the screening & triage: initial recognition of patients with symptoms associated with covid-19 infection, instantaneous execution of proper contamination's prevention & control (IPC) measures, collection of samples for laboratory testing, management of mild covid-19: indicative treatment & monitoring, management of severe-covid-19: oxygentherapy & monitoring, management of severe covid-19: treatment of associated infections, management of lifecovid-19: threatening acute-respiratory distress syndrome (ARDS), management of critical infection and covid-19: prophylaxis of complications, management of critical infection and covid-19: septic-shock, adjunctive remedies for covid-19: corticosteroids, care of pregnant women with covid-19, care of infants & breastfeeding mothers with covid-19: IPC and care of aged persons with covid-19.

Previously, Convalescent plasma or immunoglobulins were used to enhance the rate of survival in SARS patients. The condition of these patients continued to worsen after treatment with methylprednisolone. Several studies reflect a shorter stay at hospital as well as lower mortality in patients treated with Convalescent plasma or immunoglobulins [23-25]. Published researches have attracted towards the probable therapeutic benefits of chloroquine in the treatment of COVID-19. Scientist should reflect this ignition towards the development of novel antiviral against COVID-19 in consideration with previous experimentation on chloroquine [26]. Lopinavir-Ritonavir treatment in adults hospitalized with severe COVID-19 remains ineffective beyond standard care [27]. Ruxolitinib, Baricitinib and fedratinib, indicated for myelofibrosis & rheumatoid arthritis, are suggested to decline the level of interferon- γ observed in COVID-19 patients [28]. Some studies have claimed the apparent efficacy & safety of antimalarial drug chloroquine phosphate against associated pneumonia in COVID-19 patients. Study suggested the inclusion of chloroquine phosphate by the National Health Commission of the People's Republic of China in their guidelines for the prevention, diagnosis & treatment of pneumonia caused due to COVID-19 [29, 30]. Azithromycin, a macrolide antibiotic, significantly synergized the efficiency of hydroxychloro-quine, belonging to antimalarial category, for the elimination of corona virus [31]. In absence of the specific antiviral immunomodulatory therapy for COVID-19, & Numerous infected patients described that they have been tried with potentially targeted therapies like corticosteroids & neuraminidase. A very few patients have been enrolled in clinical trials [32]. No scientific

evidence is up to now available to support the chance of vertical spread of COVID-19 contamination from the pregnant mother to the baby [33, 34].

Sustaining staff's mental well-being is also essential to better control the infection of the disease, even though the best possible approach to this amid epidemic season still remains uncertain [35]. The mechanism of clearance of virus is unclear post infection and therefore required 2 weeks quarantine after getting discharge from hospital along with regular follow up. These practices achieve good result in cured patients [36]. Researchers are striving to develop specific antivirals against the virus. Quite a few drugs for example remdesivir, chloroquine, favipiravir and arbidol are presently under clinical trials to evaluate their safety & efficacy in the treatment of COVID-19 in China and some hopeful consequences have been attained so far [37].

6. VACCINATION AGAINST COVID-19

Vaccines seem to be most promising solution to attenuate newer strains of corona virus. The recognition of genomic sequence as well study of protein structure of corona virus-2019, were studied in very lesser time. This allowed the development of inactivated or live attenuated vaccine for the prevention of COVID-19 [38]. Various approaches and institutions involved in the development of vaccines are reviewed in this study.

6.1. Vaccines derived from attenuated SARS-CoV-2 viruses

As historical development of several types of vaccines is based on a living microorganism that has been incapacitated enough to cause disease. Meanwhile attenuated microbe holds the capability to replicate invivo causing a restricted disease, they are efficacious in stimulating the body's defense mechanism and bringing a robust and insistent immune retention that is effective in prevention of infection. This technology is traditionally used in development of vaccines against potentially fatal microorganisms. The oral and intranasal routes are deployed to persuade a mucosal immune potential based on IgM and IgA secretion [39]. The institutions those are working on clinical trials of attenuated-SARS-CoV-2 vaccines includes, Indian Immunologicals Limited, India, in collaboration with Griffith University, Australia [40], The Serum Institute of India in partnership with Codagenix, New York [41], Mehmet Ali Aydunar University, Turkey [42].

6.2. Vaccines originating from inactivated SARS -CoV-2 viruses

Innumerable vaccine has been developed on the principle of inactivated SARS-CoV-2 viruses (killed microorganisms). This platform produces more stable vaccines, but their limitation is short duration of immunity stimulation. Hence, this vaccination requires inoculation of elevated amount of vaccine or coadministration of attenuated SARS-CoV-2 viruses. The immune response is focused against the spike-protein along with several other antigens of SARS-CoV-2. In comparison to vaccines based on attenuated-SARS-CoV-2 viruses, the immune system is weakly induced by these class of vaccines but conversely these vaccines are based on the inactivated SARS-CoV-2 viruses are safer, easily handled and less expensive. Different chemical techniques are adopted to obtain vaccines based on inactivated-SARS-CoV-2 virus and administered intramuscularly. The institutions those are working on clinical trials of vaccines produced from this technique, includes: Bharat Biotech, India in collaboration with ICMR (Indian Council of Medical Research), India which is a government backed biomedical research institute, and its wing National Institute of Virology developing Covaxin [43], Sinovac Biotech, China is engaged in producing vaccine named as CoronaVac, although its limited used has been approved in general population [44], Sinopharm, China has been granted to use its two projects among general population [45], Wuhan Institute of Biological Products, China, vaccine got approved for the restricted use in the general community [46], Institute for Biological Safety Problems (RIBSP) in Gvardeiskiy, Kazakhstan [47] and Chinese Academy of Sciences, Beijing, China [48].

6.3. Vaccines derived from SARS-CoV-2 proteins

Many vaccines are available on the principle of proteins purified from microbes. Recombinant DNA technology is used in *in-vitro* production of such vaccines. Spike proteins and its fragments become targets of all these types of vaccines. In some other cases SARS-CoV-2 proteins, mostly nucleoprotein (N), are also targeted. The institutions those are working on clinical-trials of vaccines evolved from SARS-CoV-2 Spike protein and/or its fragments plus adjuvant are as: The University of Queensland, Australia (Vaxine) [49], USA (Covaxx)[50], Sanofi and GlaxoSmithKline, France & Italy, [51] Medigen, Taiwan [52], Bektop [53] & Biotechnology Vector, Russia [54] and University of

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Tübingen, Germany etc. Novavax, USA is working on vaccines based on Proteins carried by nanoparticles, Vaxart, USA is working on vaccines based on oral tablet containing the spike protein fragments, The University of Queensland is also working on vaccines based on micro-needle skin patch delivering spike proteins, Serum Institute of India along with SpyBiotech is developing vaccines based on spike protein or its fragments implanted in virus-like particles (VLP) [55], Medicago in association with GSK is working to develop vaccines based on tobacco's plantproduced proteins in virus-like particles (VLP) whereas Kentucky Bio Processing, USA is in progress to develop Vaccines based on tobacco plant produced proteins [56].

6.4. Vaccines based on Naked DNA

DNA and mRNA-based technology provide higher flexibility. As of now, no DNA based vaccine is registered for clinical use. DNA vaccination is most employed in veterinary medicine. Such vaccines under clinical trial are being developed by AnGes, Japan, Takis, Italy and Zydus Cadila, India [57]. Beside these, Genexine, Korea, Karolinska institute, Sweden along with Inovio, Italy are in phases of developing vaccines based on naked DNA plasmids plus electroporation [39].

6.5. Vaccines based on mRNA

RNA is transported to enter human cells by means of several mechanisms. As soon as entered, the mRNA vaccine momentarily encourages the cell to yield antigen protein those are coded by mRNA. mRNAbased vaccines are under clinical trials by Moderna, USA, CureVac, Germany, Abogn, China, BioNTech, USA & Pfizer and Oxfrod University, UK [58]. Additionally, Arcturus Therapeutics, Singapore is trialing its nanoparticle-based mRNA vaccine [59].

6.6. Vaccines based on viral vectors

The DNA-coding for the spike protein may be transported into the cells by the viral vectors. By implanting DNA in a virus, it is likely to exploit the great ability of virus to infect and carry the mRNA into the cells of human [60]. Vaccines based on viral vectors under trials include the under-trial vaccines of Astra Zeneca in association with Oxford University in Sweden-Italy-UK based on chimpanzee adenovirus. Rei Therapeutics, Italy is working on a vaccine to be developed from Gorilla adenovirus. Apart from these, Johnson & Jonhson, USA, Academy of military medical sciences, China and Gamaleya Research Institute, Russia are working on vaccines from human adenoviruses as viral vector. Additionally, Astra Zeneca, Sweden; Bharat Biotech, India in association with Washington University, USA are also developing modified adenovirus specifically for nasal spray. Other virus including measles virus (Merck, US), Influenza virus (University of Hongkong) are also engineered as replicating virus vector [61].

6.7. Vaccination approved for current emergent use

Apart from above discussed ongoing clinical trials to develop vaccine against COVID-19, a very few has been approved and being used based on their proven efficacy as well as non-significant adverse events. The reviewed information regarding vaccines currently in used is summarized in the table 1.

Table 1: Vaccines	being used	after getting	emergency approval

Vaccine name	Developed by	Countries approved the vaccine	Туре	Efficacy rate	Side effect(s)
Covaxin (BBV152) [62]	Bharat Biotech, India in association with National Institute of Virology, a major wing ofIndian council of Medical Research, India.	Iran Philippines Mauritius Mexico Nepal Guyana Paraguay Zimbabwe India.	Whole- Virion Inactivated Vero Cell- derived platform	The updated second interim phase 3 trial data show that Covaxin has an efficacy rate of 78%, a tad lower than the earlier reported efficacy of 80.6% based on the first interim trials conducted in March. The effectiveness against severe COVID-19	Some mild symptoms like pain& swelling at injection site, fatigue, headache, body ache, fever, nausea & vomiting, dizziness- giddiness, abdominal pain, sweating, tremor, cough &cold. No other vaccine related serious adverse effect have

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		Afghanistan		disease was 100% as the company claimed. But efficacy against asymptomatic COVID- 19 infection was found to be 70%. The vaccine can induce antibodies that can counteract even the U.K., Brazilianand other different strains of COVID-19.	been reported so far.
Covishield (AZD1222) [63]	Serum Institute of India in partnership with Oxford University, UK.	Argentina Argentina Bhutan Antigua Bahrain Bangladesh Egypt Canada Brazil Ghana Ethiopia Hungary Grenada India Maldives Jamaica Morocco Nepal Namibia Nigeria South Africa Somalia Sri Lanka Ukraine Tonga and others	Viral vectorplatf orm	The peer-reviewed results of the Phase-III trials of the Covishield show that it is up to 90% effective. The results also revealed that the vaccine was only 62% effective when participants were given two full doses, but its efficacy rose to 90% when a half-dose followed by a full dose was administered. Likely, the vaccine will be effective against the new strain as well. Covishield works effectively against the UK strain and is being tested against the Brazilian variant.	Covishield does have a few side effects, such as pain, redness, itching, swelling or bruising, feeling unwell, fatigue, chills, fever, headache, nausea, joint pain, and muscle ache, but they are mostly mild to moderate in nature and can be treated with over-the-counter pills. It is also known to have triggered shortness of breath, swelling of the face or tongue, allergic reactions like itchy skin-rash, and with a history of allergies, it is advised to consult with doctor first.
Sputnik-V [64]	The Gamaleya Research Institute of Epidemiology and Microbiology, Russia.	Albania Algeria Angola Antigua and Barbuda Argentina Argentina Azerbaijan Bahrain Bangladesh Belarus Bolivia Bosnia and Herzegovina Cameroon Egypt Ghana	Sputnik is also a vector vaccine, based on an adenovirus. It consists of an engineered virus without the ability to replicate or multiply, which when injected	Manufacturers of the Sputnik V vaccine released a statement detailing an impressive 95 percent efficacy rate. Calculations were based on the analysis of data on volunteers received both first & second doses of the Sputnik- Vor placebo at the second control-point according to the clinical trial decorum. Preliminary data from volunteers obtained 42 days after the first dose	Short term minor adverse effect like flu- like symptoms & pain at the injection site including fever, weakness, fatigue, and headache. During trials no severe adverse event was reported. It should not be administered to anyone in an acute stage of allergic reaction. One should get blood tests done for Immunoglobulin E

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		Guinea Guyana Hungary India United Arab Emirates Iran Uruguay Iraq Jordan Kazakhstan Kenya Myanmar Lebanon Libya Malaysia Pakistan Morocco Maldives Thailand Mauritius Mexico Mongolia Namibia Turkey Nepal Philippines Syria Russia Serbia Sri Lanka Tunisia Venezuela Vietnam Zimbabwe and more.	into the human body, triggers an immune response to the corona- virus spike proteins. The regimen comprises two doses to be administere d 28 days apart. Like its Indian counterpar ts, Sputnik too remains stable at 2- 8 degrees celsius.	or 21 days after the second dose indicates Sputnik V's efficacy is above 95 percent. According to the makers of the vaccine, Sputnik is one of the best options against the mutations of the virus as it is the only one that uses two totally different shots.	and C-reactive protein in case of allergies, and if they aren't within the normal limit, they should reconsider getting the Sputnik jab.
Pfizer- BioNTech COVID-19 Vaccine (BNT162b2) [65]	Pfizer, Inc., and BioNTech	United Kingdom Bahrain Canada Saudi Arabia Mexico	mRNA vaccine	Pfizer-BioNTech vaccine was found to be 95% effective at preventing laboratory- confirmed COVID-19 illness in people without evidence of previous infection during clinical trials performed in the peoples of age of 16 years and older	Symptoms at the site of injection includes swelling, redness, and pain. System side effects includes headache, tiredness, fever, muscle pain, chills & nausea.
Moderna (mRNA-1273) [66]	Moderna, TX, Inc.	United States, the European Union, Canada, Israel, Singapore and United	RNA vaccine [composed of nucleoside- modified mRNA	Clinical trials showed 94.1% efficacy in the prevention of laboratory confirmed COVID-19 infection in the peoples who received two doses and	Symptoms at the site of injection includes swelling, redness, and pain. System side effects includes headache, tiredness, fever,

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		Kingdom.	(modRN) encoding a spike protein of SARS- CoV-2] which is encapsulate d in lipid nano- particles.	had no evidence of being infected previously.	muscle pain, chills & nausea.
Johnson& Johnson's Janssen COVID-19 Vaccine (JNJ-78436735) [67]	Janssen Pharmaceuticals Companies of Johnson & Johnson	Europe Africa United States, Canada United Kingdom, Colombia South Korea Chile New Zealand	À harmless adenovirus, the viral vector, and substituted a small piece of its genetic informatio n with coronavirus genes for the SARS- CoV-2 spike protein.	Vaccine was found to be 66.3% effective in clinical trials2 weeks after receiving the vaccine in the prevention of laboratory confirmed COVID-19 infection in the people had no evidence of previous infection. People had the most protection 2 weeks after getting vaccinated.	Symptoms at the site of injection includes swelling, redness, and pain. System side effects includes headache, tiredness, fever, muscle pain, chills & nausea.
Sinopharm (Beijing) [68]	Sinopharm's Beijing Institute of Biological Products, China	UAE, Peru, Argentina, Bahrain, Jordan, Egypt	Inactivated virus	79-86% (2 doses)	Headaches Fatigue injection site reactions These side effects are like those of other authorized vaccines against COVID-19, and most were mild to moderate.
Sinopharm (Wuhan)[69]	Sinopharm's Wuhan Institute of Biological Products, China	UAE, Peru, Bahrain, Jordan, Egypt, Morocco	Inactivated virus	73% (2 doses)	Headaches fatigue injection site reactions These side effects are like those of other authorized vaccines against COVID-19, and most were mild to moderate.
CoronaVac [70]	Sinovac Biotech, China	Chile, Indonesia, Brazil, Turkey, Philippines, China	Inactivated virus	50-84% (2 doses)	Blood Pressure Increase Headache Vaccination site pain Dizziness Rash
Convidecia [71]	CanSino Biologics; Academy of Military Medical Sciences, China	Pakistan, Russia, Chile, Argentina, Mexico	Adenovirus vector	65-69% (1 dose)	Headache Vaccination site pain Dizziness Rash

7. CONCLUSION

Remarkable development of treatment options has improved the recovery and mortality from Covid-19 induced pneumonia. Scientifically proven clinical data enables to the tailored therapies based on improving the outcomes in patients. Development of vaccine is a timeconsuming finding varying from 10 to 15 years. Availability of modern technology and collaborative efforts as well as active participation of regulatory bodies concluded the approval of vaccine against Covid-19 after only 9 months of the prevalence of disease. BioNTech COVID-19 Vaccine (BNT162b2), Moderna (mRNA-1273), Johnson& Johnson's Janssen COVID-19 Vaccine (JNJ-78436735), Sinopharm (Beijing), Sinopharm (Wuhan), Corona Vac, and Convidecia are few examples of vaccines currently in use by diverse countries. These vaccines have not only been used in originated countries while these has been approved by various other countries. Whole-Virion Inactivated Vero Cell-derived platform, Viral vector platform, vector vaccine, based on an adenovirus, RNA vaccine [composed of nucleoside-modified mRNA (modRNA) encoding a spike protein of SARS-CoV-2] and Inactivated virus are the platforms on which these vaccines have been developed. Collectively, these vaccines have mild side effects like pain & swelling at injection site, fatigue, headache, body ache, fever, nausea & vomiting, dizziness-giddiness, abdominal pain, sweating, tremor, cough & cold. Severe side effects have not been reported by any of these vaccines so far. The conducted studies have confirmed the partial to complete effectiveness of some currently used vaccines in the prevention of Covid-19. In cases of emergence of various mutants, these vaccines need to be updated accordingly in future either by designing the multivalent type vaccines or matching the existing strain to widen the spectrum.

Conflict of Interest

None declared

8. REFERENCES

- Sun P, Lu X, Xu C, Sun W, Pan B. Journal of medical virology. 2020 Jun; 92(6):548-551.
- Russell CD, Millar JE, Baillie JK. The Lancet. 2020; 395(10223):473-475.
- Wang LS, Wang YR, Ye DW, Liu QQ. Inter J Antimicrob Agents. 2019; 30(1):105-108.
- Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et.al. New England journal of medicine. 2020; 24: 10-12.

- Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. *Nature*, 2020; 579(7798):270-273.
- Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et. al. *The lancet*. 2020; **395(10224):**565-574.
- Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, et al. *Military Medical Research*, 2020; 7(1):1-10.
- WHO. (2020). Coronavirus disease 2019 (COVID-19) situation report-51.
- Cascella M, Rajnik M, Aleem A, Dulebohn S, Di Napoli R. StatPearls, 2021; 20(1):1-4.
- WHO. (2020). Coronavirus disease 2019 (COVID-19) situation report-56.
- 11. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. New England journal of Medicine. 2020; 29.
- 12. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. *The lancet*, 2020; **395(10229):**1054-1062.
- Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, et al. *Emerging microbes & infections*, 2020; 9(1):221-236.
- 14. Chan JF, To KK, Tse H, Jin DY, Yuen KY. *Trends* in *Microbiology*, 2013; **21(10):**544-555.
- Chen Y, Liu Q, Guo D. Journal of Medical Virology. 2020; 92(4):418-423.
- Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. *The Lancet respiratory Medicine*, 2020; 8(4):420-422.
- 17. Perlman S, Netland J. Nature reviews microbiology, 2009; 7(6):439-450.
- 18. Lei J, Kusov Y, Hilgenfeld R. Antiviral research, 2018; 149:58-74.
- 19. Fang L, Karakiulakis G, Roth M. The Lancet. Respiratory Medicine. 2020; 8(4):e21.
- Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. *The lancet*, 2020; 395 (10229):1033-1034.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. *The lancet*, 2020; **395(10223)**:507-513.
- 22. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. *The Lancet infectious diseases*, 2020; **20(4)**:425-434.
- Lai ST. European Journal of Clinical Microbiology and Infectious Diseases. 2005; 24(9):583-591.
- Soo YO, Cheng Y, Wong R, Hui DS, Lee CK, Tsang KK, et al. *Clinical microbiology and infection*. 2004; **10(7):**676-678.
- Cheng Y, Wong R, Soo YO, Wong WS, Lee CK, Ng MH, et al. European Journal of Clinical Microbiology and Infectious Diseases, 2005; 24(1):44-46.
- Touret F, de Lamballerie X. Antiviral research, 2020; 177:104762.
- 27. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G,

Ruan L, et al. New England Journal of Medicine, 2020; 382:1787-1799.

- Stebbing J, Phelan A, Griffin I, Tucker C, Oechsle O, Smith D, et al. *The Lancet Infectious Diseases*, 2020; 20(4):400-2.
- Gao J, Tian Z, Yang X. Bioscience Trends, 2020; 14(1):72-73.
- 30. Cortegiani A, Ingoglia G, Ippolito M, Giarratano A, Einav S. *Journal of critical care*, 2020; **57:**279-283.
- Gautret P, Lagier JC, Parola P, Meddeb L, Mailhe M, Doudier B, et al. *International journal of antimicrobial agents*, 2020; 56(1):105949.
- Murthy S, Gomersall CD, Fowler RA. Jama, 2020; 323(15):1499-1500.
- 33. Qiao J. The Lancet, 2020; 395(10226):760-762.
- Lu Q, Shi Y. Journal of medical virology, 2020; 92(6):564-567.
- 35. Chen Q, Liang M, Li Y, Guo J, Fei D, Wang L, et al. *The Lancet Psychiatry*, 2020; **7(4)**:e15-16.
- Xu K, Cai H, Shen Y, Ni Q, Chen Y, Hu S, et al. Journal of Zhejiang University (medical science), 2020; 49(1):1-5.
- 37. Dong L, Hu S, Gao J. Drug discoveries & Therapeutics. 2020; 14(1):58-60.
- Shin MD, Shukla S, Chung YH, Beiss V, Chan SK, Ortega-Rivera OA, et al. *Nature nanotechnology*, 2020; 15(8):646-655.
- Forni G, Mantovani A. Cell Death & Differentiation, 2021; 28(2):626-639.
- Pagliusi S, Jarrett S, Hayman B, Kreysa U, Prasad SD, Reers M, et al. *Vaccine*, 2020; **38(34):**5418-5423.
- 41. Chakraborty C, Agoramoorthy G. Vaccine, 2020; 38(50):7883.
- 42. Dei Lincei, A. N. COVID-19 vaccines: Fall 2020 report.
- PuŚlecki Ł, Dąbrowski M, PuŚlecki M. European Research Studies, 2021; 24:1049-1073.
- 44. Kyriakidis NC, López-Cortés A, González EV, Grimaldos AB, Prado EO. *Vaccines*, 2021; **6(1)**:1-7.
- 45. Kim JH, Marks F, Clemens JD. Nature medicine, 2021; 27(2):205-211.
- Yan Y, Pang Y, Lyu Z, Wang R, Wu X, You C, et al. *Vaccines*, 2021; 9(4):349.
- Wouters OJ, Shadlen KC, Salcher-Konrad M, Pollard AJ, Larson HJ, Teerawattananon Y, et al. *The Lancet*, 2021; **397(10):**1023-1034.
- 48. Huang B, Dai L, Wang H, Hu Z, Yang X, Tan W, et al. *The Lancet Microbe*, 2021; **2(2):**12-16.
- 49. McIntyre P, Joo YJ, Chiu C, Flanagan K, Macartney

K. Australian Prescriber, 2021; 44(1):19.

- Feng G, Zhang L, Wang K, Chen B, Xia HH. Journal of Exploratory Research in Pharmacology, 2021; 6(2):31-43.
- 51. Watson SI, Lilford RJ. The Lancet, 2021; **397** (10287):1804-1805.
- 52. Wang WC, Fann JC, Chang RE, Jeng YC, Hsu CY, Chen HH, et al. *Journal of the Formosan Medical* Association, 2021 May 25; **120(1)**:S95-S105.
- 53. O'Shea J, Prausnitz MR, Rouphael N. Vaccines, 2021 Apr; 9(4):320.
- 54. Hsieh SM, Liu WD, Huang YS, Lin YJ, Hsieh EF, Lian WC, et al. *The lancet*, 2021; 1018.
- 55. Belete TM. Infection and drug resistance, 2021; 14:151.
- Kumar AU, Kadiresen K, Gan WC, Ling AP. Clinical and Experimental Vaccine Research, 2021; 10(1):13.
- 57. Choudhary HB, Sirvi IH, Bamb YR, Bamb PR, RajkumarPatekar R. World Journal of Advanced Research and Reviews, 2021; **10(1):**143-155.
- Khurana A, Allawadhi P, Khurana I, Allwadhi S, Weiskirchen R, Banothu AK, et al. *Nano Today*, 2021 Jun 1; 38:101142.
- Misra SK, Pathak K, Pathak D, Yadav R. Asian Journal of Pharmaceutical and Clinical Research, 2021 Mar 7:17-23.
- Catania LJ. Foundations of Artificial Intelligence in Healthcare and Bioscience, 2021; 13(30):445.
- 61. Lundstrom K. Viruses, 2021 Feb; 13(2):317.
- Sapkal GN, Yadav PD, Ella R, Deshpande GR, Sahay RR, et al. *Journal of Travel Medicine*, 2021; 28(4):51.
- 63. Thiagarajan K. BMJ Journals, 2021; 372:n196.
- 64. Jones I, Roy P. The Lancet, 2021; **397(10275)**:642-643.
- Bernal JL, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, et al. *BMJ Journals*, 2021; 23(343):373.
- 66. Thompson MG, Burgess JL, Naleway AL, Tyner HL, Yoon SK, Meece J, et al. *Morbidity and Mortality Weekly Report*, 2021; **70(13):**495.
- 67. Oliver SE, Shimabukuro TT. The lancet, 2021; 3:4.
- 68. Baraniuk C. *Bmj journals*. 2021; 373.
- 69. Burgess LH, Castelein C, Rubio A, Cooper MK. *Healthcare Journal of Medicine*, 2021; **2(2):**2.
- 70. Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, et al. *The Lancet infectious diseases*, 2021; **21(2):**181-92.
- 71. Yan ZP, Yang M, Lai CL. *Pharmaceuticals*, 2021; **14(5):**406.