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VACCINATION STRATAGEMS TO COMBAT CORONA VIRUS

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ABSTRACT

Pandemic caused due to Corona virus in last two years has created lot of havoc and casualties. The evolutionary pathway for corona virus is mutating with recombination, convergence and adaptation. Most research papers reported that the poly basic protein cleavage site and mutation of genetics of the spike proteins are the main culprits behind the adaptation of beta coronavirus group of SARS-COV-2 to humans. Vaccines have tremendous potential to fight against viral diseases as they have dominances in safety, efficiency. In last three years we have witnessed the experiments and trials and development of different kinds of vaccines to combat against SARCov-2. Based on the different researches conducted in different countries suitable vaccines are produced coupled with immunologic adjuvant and various delivery strategies. This current review concludes, with all conceivable knowledge about structure of corona virus, target protein for vaccine development and availability of vaccines and new ongoing clinical trials for children's vaccines. The challenge to prevent unvaccinated group of children from corona virus and its consequences is critical.

Keywords: SARSCOV-2, Covid vaccine, S-protein, spike protein,

Introduction

Viruses are non-predictive organisms in behaviour. Being outliers of living and non-living kingdom, they have potential of life threatening and may be cause to irretrievable loss to human species. When we are able to cope with one kind or strain of virus then another pops up and start its thunder like a robust version of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that has been claimed to be also artificial/synthetic [1]. The evolutionary pathway for SARS-COV-2 is revolving around recombination, convergence, and adaptation [2]. Most research papers reported that the poly basic protein cleavage site and mutation of genetics of the spike proteins are the main culprits behind the adaptation of beta coronavirus group of SARS-COV-2 to humans [3]. Moreover, evidences of the similarity between SARS-COV-2, bat-coronavirus, and pangolin-coronavirus at the genomic level have also been discovered. The S1-2 junction of coronavirus is altered by mutations, insertions, and deletions in genetic sequences, depicting that the production

of polybasic cleavage sites via evolutionary process occurring in virus [3].

Coronaviruses (CoVs) are single unit with no segments, enveloped with single-strand, positive, RNA acid viruses fitting to the Coronaviridae family. CoVs named due to the crown-like surface projections seems to represent sun like radiation. CoVs are host-specific RNA viruses based that can infect many species including humans. CoVs are classified into a) Alpha and Beta affecting bats, rodents, and homosapiens b) Gamma and Delta which are mostly found in birdies [4].

There were three CoVs recognised so far as to cause severe respiratory infections. These are named as SARS-COV which emerged in 2002, MERS-COV occurred in 2012, and SARS-CoV-2 that was responsible for COVID- 19 disease 2019 and obtaining a global health pandemic status by the World Health Organization (WHO) [5]. WHO dashboard as on 29 July 2022, 5:33pm CEST, declares 572,239,451 confirmed cases of COVID-19, including 6,390,401 deaths. An aggregate of 12,248,795,623 vaccine doses have been administered on 25 July 2022.

Table 1: Several members of the Corona-viridae family infect humans. [6,7]

Common human coronaviruses	**Other human coronaviruses**
229E (alpha coronavirus)	MERS-CoV (the beta coronavirus - Middle East Respiratory Syndrome)
NL63 (alpha coronavirus)	SARS-CoV (the beta coronavirus - severe acute respiratory syndrome)
OC43 (beta coronavirus)	SARS-CoV-2 (coronavirus disease 2019, or COVID-19)
HKU1 (beta coronavirus)	

Elements of CORONA virus

The Covid virus has about 30 (26-32) kb pairs in its genome structure. The virus encodes several non-structural proteins (NSP) attached to its structure. The Covid-2 virus contains four organisational proteins which involves Membrane glycoprotein (M), and nucleocapsid protein (N),S-spike Protein and envelope protein (E), that augment attachment, transport and restricts with host immune responses. These proteins aid the virus-host cell interactions to create an optimum environment for viral replication, neutralization of the host's antiviral defences system. The viral disease pathogenesis is due to these virus –host attachment [8]. The S protein (transmembrane glycoprotein) endorses the ingress of the virus into healthy cells. S protein has become chief target of approach for making scheme for successful vaccines and chief inhibitors for virus entry. The S protein includes two domains namely S1 and S2. The S1 contains the receptor binding domain (RBD) that facilitates addition to the host receptor cell, whereas the S2 smoothen /eases the fusion of the virus to the host cell.

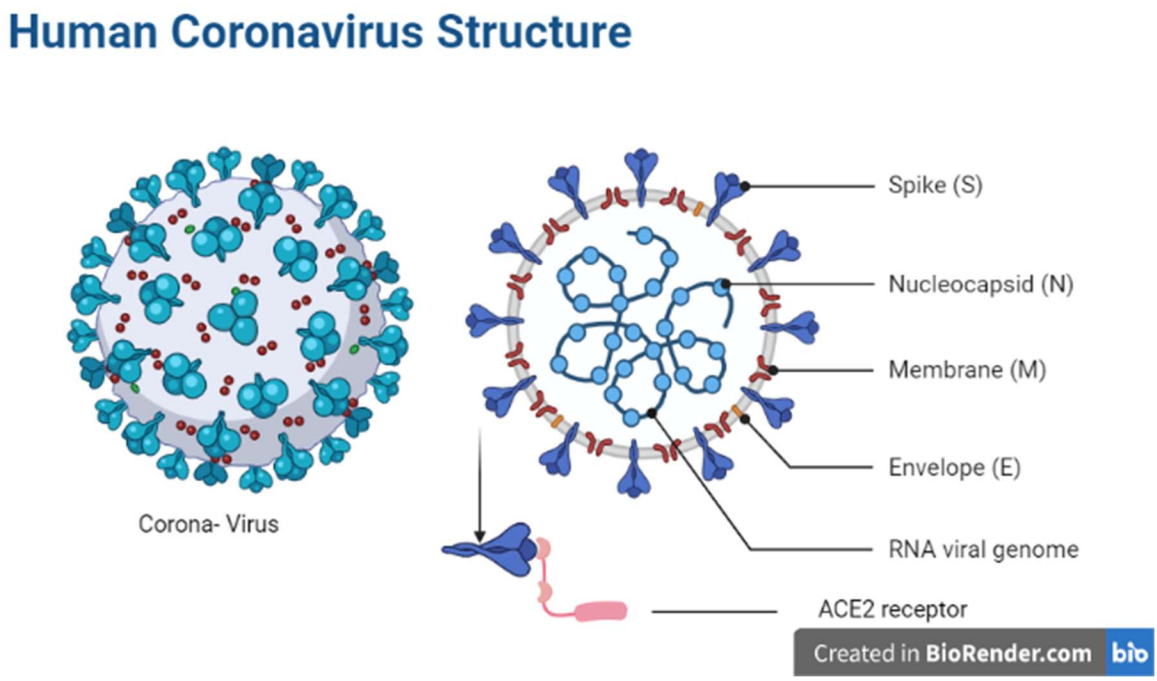

Figure1: Adapted from "HUMAN CORONA VIRUS", by BioRender.com (2021). Retrieved from https://app.biorender.com/biorender-templates

Interaction of the RBD with angiotensin-converting enzyme 2 (ACE2) initiates the entry of SARS-CoV-2 into receiver or host cells . ACE2 is found to be the primary receptor of corona infection on the receiver cells surface. ACE2 receptors are usually articulated in type II alveolar cells, epithelium of air passage, immune cells and many more types of cell in our tissues . S2 subunit facilitates the viral envelope and cell membrane merging by presenting its domain. This domain of S2 contains inner membrane fusion peptide (FP), a transmembrane domain (TM) ,membrane proximal external region (MPER), and 7- peptide repeats. In this infection the S glycoprotein has vital role in the stimulation of host immune responses and triggering immunity by neutralizing-antibodies and enhancing T-cell responses. Researches have shown that the RBD located in the S1 region is a powerful stimulator of neutralizing antibodies. Therefore, the S1 subunit, the RBD domain,full-length S glycoprotein, NTD, and FP are anticipated as the hopeful candidates for an effective vaccine against SARS-CoV-2.[9,10]

The M- protein present in structure of SARCOV 2 is a transmembrane glycoprotein who works as definite shape provider to the virus structure. It attaches to nucleocapsid and systematises the virus assembly. The E protein inactivation alters the virulence of CoVs via morphological and tropical alterations. The N-nucelocapsid protein present inside phospholipid bilayer , participates in formation of multifaceted complex with viral genome, augments M protein interaction during assembly, and upsurges imitation of the virus. Altogether proteins (E,S,M) comprises the outer shell of the viral envelope[10].

Sars-Cov-2: Podiums for vaccine development

SARS-CoV-2 Vaccines may decrease disease severity, viral flaking, and communicable transmission. Therefore, making them vital need for controlling the pandemic [11]. Vaccines are developed on the different base that may be any one of the following: live attenuated virus (LAV), inactivated virus, recombinant DNA, viral vectors, protein vaccines or subunit vaccines. Several studies depicted viral S protein subunit vaccines tend to have higher potencies of neutralizing antibody titres and defence than LAV against SARS-CoV, and DNA-based S protein vaccines. Jointly, S protein/gene was the desired target site in this pandemic for vaccine invention, and the similar strategy was advantageous in developing SARS-CoV-2 vaccine [11,12]. The WHO classification for COVID-19 vaccines into the following categories (such as an inactivated vaccine, live attenuated, vector, RNA, DNA, protein subunit, and virus-like particle vaccines) were approved for clinical trials.

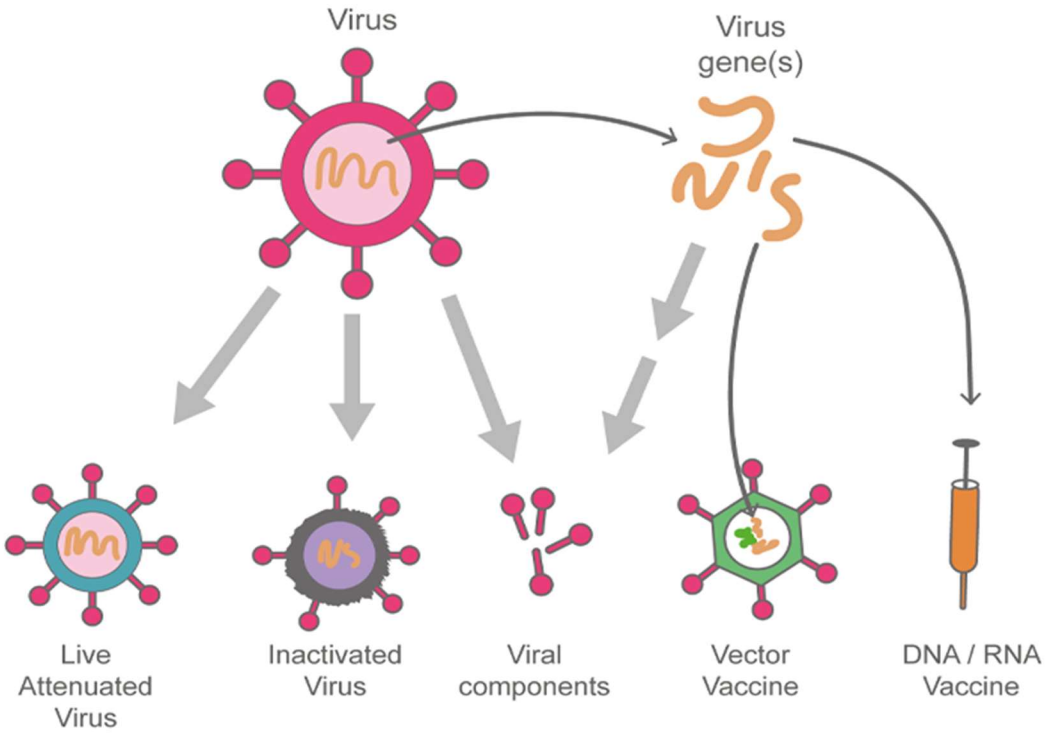

Figure2: Various modes of vaccination [13]

1. **Live-Attenuated Vaccines (LAV)**

LAV is the most immunity producing type of vaccines. LAV is just like natural infection thus it do not require adjuvant to increase optimal response due to its efficacy to aggravate immunity. The LAV comprehend sustainable but tempered live virus with low virulence property so that it is not able to cause disease in individuals with non-compromised immune systems. They productivity is slowed down, and it becomes a unceasing source of antigen production for a extended period [14]. To protect mumps, rubella, measles and varicella vaccines many LAV are found. LAV is

synthesized by many techniques involving: virus processing in cell cultures, in model including animals or restraining them at less than ideal temperatures. Then the weakened virus is selected by less virulent type selection or by mutated virus selection, or deletion of the specific viral genes that give potency of virulence [15].

Codagenix Biotec collaborated with the Serum Institute of India to develop LAV, SARS-CoV-2 vaccine where sequence codings of the " gene of target" has been transformed by exchanging its optimized codons with non-optimized ones[16]. Inactivated Whole-Virus (IWV) Vaccine comprises of the entire disease-causing virus which is inactivated either physically (heat) or chemically. It has numerous antigenic parts to the host and can induce diverse immune responses against the pathogen. IWV is superior to other type of vaccines due to low cost, safety, and no genetic manipulation[17].

2. Vaccines based on Subunit

Subunit vaccines contain antigens which are pathogen created proteins with immunity spawning potential to trigger host immune system. Subunit vaccines can be developed by recombinant DNA techniques but demands adjuvant to augment an immune response. Many research institutions had begun the SARS-CoV-2 subunits to create vaccine, and also by using the spike glycoprotein S or its fragments (S1, S2, RBD, and nucleocapsid protein) making them supreme target antigens for S protein based vaccine development. Clover Biopharmaceuticals applied its patented Trimer-Tag tool technology to construct a SARS-CoV-2 S protein trimer vaccine (S-Trimer) [18]. RBD immunization induces precise antibodies due to binding effect of ACE2 and RBD of S protein that can block recognition of ACE2 of host to RBD of virus and can effectively prevent the incursion of the virus.

Vaccine developed against COVID-19. In India, COVAXIN and COVISHIELD have been approved for the purpose to combat pandemic by the Drug Controller General of India (DCGI). Until now administrated total vaccinationdoses **2100240361 in India as updated on 22 august 2022**.The World Health Organization (WHO) advisory experts on Immunization has recommended the use of the Oxford-Astra Zeneca vaccine (AZD1222) in person having comorbidities, identified as increasing the risk of severe COVID-19(hypertension, asthma, diabetes mellitus ,obesity and cardiovascular diseases) [19]. The initial supplies of COVID-19 vaccine were allocated to healthcare staffs and long-standing care facility residents referring to as Phase 1a. Subsequently, vaccination was provided as a part of Phase 1b and Phase 1c. Phase 1c had persons of aged 16-64 years with comorbities underlying like T2D as one of the medical conditions[20]. The Diabetes UK, vaccination in patients with DM were preferred [21]. Vaccination for children has started with Pfizer-BioNTech, Moderna or Spikevax COVID-19 vaccine as emergency use instructions as issued by the Centre for Disease Control and Prevention (CDC) and approved by FDA. Children's age group 12 years and older and some higher risk groups like immunocompromised, myocarditis children were recommended to get two doses in between 3-8 weeks gap. However, none of these vaccines has been tested in children <11 years of age.

Mechanism and mode of action among vaccine candidates

The most significant vaccines provoke long-standing antigen-specific responses by plasma cell antibodies other than the growth of persevering T cell and B cell memory. In case of corona infection, treatment and cleansing both humoral and cellular immune responses are required. Vectors of recombinant technology slog in like an analogous to endogenous pathogen causing organism. Thereby expressing target protein in cytoplasm of the host cell. After, processing, MHC class 1 particles present them to CD8+ T-lymphocytes, leading to production of T-cytotoxic cells. This corridor, primes to establishment of cell-mediated immune up raiser, which is critical in swiping of virus infected cells. Sub unit vaccine candidate predominantly RBD of SARS-CoV contains chief antigenic determining factor that can persuade neutralizing antibodies [22]. The S protein is capable of inducing CD8+ T-cell responses. The RBD comprises multiple epitopes for binding and becomes crucial domain of persuading neutralizing antibodies against SARS-CoV infection [23,24] making it favourable target for vaccine. Adenoviral vectors are also similarly capable to persuade potent antibody in addition to T cell responses [25]. Among all replication-deficient Ad5, is most widely used adenoviral vectors, having both the above qualities of antibody and T cell response generation [26]. Additionally DNA dependent vaccine can activate CD8+ cytotoxic besides CD4+ helper T cells, introducing both kind of immune responses. However, injection of S protein encoding DNA vaccine provoked protective immunity against SARS-CoV infection in rodents model via T cell induction and generation of antibody responses [27].

Nucleotide based vaccine on Exogenous mRNA is too efficient immune stimulator, as it is recognized by diverse kind of cell surface, like innate immune receptors present in cytoplasm and endosomes. Mammalian cells have potential to identify foreign RNA thru Pattern recognition receptors (PRRs) present in the endosomes (TLR3, TLR7 and TLR8) and in cytoplasm (RIG-I, MDA-5 and PKR) [28]. Instigating PRRs via mRNA vaccines outcomes in vigorous innate immune response complimenting chemokines and cytokines (IL- 12 and TNF) [29], which are innate factors critical for the induction of an active immune response in contrast to the encoded antigen. The mRNA vaccines are responsible to accumulate an immunological stock associated with the generation of high magnitude enduring antibodies [30].

Various Vaccine nominees

Viral kingdom had shown their power by emerging into epidemics in recent years and appearance of novel strains from their biological hosts makes them grim to predict [31,32]. Previous, CoV were weak in case of humans triggering mild flu-like illness nevertheless with consistent bursts like SARS and MERS in (2002,2012) respectively with present COVID-19 their capacity of virulence is well established universally [33,34].Among areas explored for the hunt of an idyllic vaccine against SARS-CoV, embraces many types of vaccines likerecombinant viral, inactivated virus , subunit, DNA based or attenuated vaccines [35].

1) Germany/United States of America- BioNTech/Pfizer

A BNT162b1 and BNT162b2 vaccine are illustrations based on mRNA manufactured by the German company BioNTech and Pfizer, in this process a synthetic mRNA is introduced into host cell and translated into protein. mRNA class of remedies are relatively fresh that deliver genetic data [36]. Treatment based on these drugs are considered harmless because the RNA is

ephemerally expressed, metabolized rapidly, and do not incorporate into the host genome [37]. An additional asset of Rna based vaccine is the capability to swiftly produce large number off vaccine against novel pathogens [36]. BNT162b1 encrypts the trimerized RBD of the spike protein with addition of T4fibritin domain. BNT162b2 encrypts the membrane-secured spanning spike protein, which is altered by two proline mutations to maintain prefusion state of stability [38]. The delivery of the mRNA into the cytoplasm is supported through a cationic lipid nanoparticle consisting of ionizable amino lipid, phospholipid, cholesterol, and a polyethylene glycol-lipid [39]. BNT162b1 produced immunity well by RBD-binding IgG antibody and T cell [CD8(+) and CD4(+)) response] [40]. The response of BNT162b2 was comparable, nevertheless this vaccine was associated with milder systemic reaction producing capacity (e.g., fever, fatigue, headache, grade 4 severe reactions) principally in the elders of 65–85 year age group [41].

Total 43,448 participants were enrolled for testing all three phases of trials of BNT162b1 and BNT162b2 . BNT162b1 is a nanoparticle-formulated with lipid, m RNA modified vaccine that encrypts the trimerized RBD of the spike glycoprotein against SARS-CoV-2.In several groups, volunteers were tested with two doses of m intramuscularly injection, age was 12-85 years. Neutralizing antibodies as well as anti-RBD binding antibody levels were measured for SAR-cov 2 serum. Two shots of BNT162b1 given in 45 adults (ages 18 - 55) verified that this vaccine lead to vigorous immunogenicity. After 7 days of second dose of 30 g of BNT162b1, which was given after interval of 21 days of first dose, resulted in amplified IgG to 27,872 U/mL which continued in subsequent week. In contrast, human recuperating sera only contained 602 U/mL of RBD-binding IgG. Similarly, SARS CoV-2 neutralizing titres were found to be 437 after 14 days of the second dose, when compared to human recuperating sera it was only 94. Symptoms on injection site were mild to moderate pain, overall fatigue and headache. Reactive symptoms improved normally after two days. During the phase III trial element of NCT04368728 documented eight cases of COVID-19 in participants receiving BNT162b2 vaccine and 162 cases among those who received the placebo [42]. This was remarkable as it was 95% effective. BioNTech/Pfizer had received emergency use authorization (EUA) from the FDA [43] [44].

2) United States of America -Moderna Vaccine

Moderna manufactured mRNA-1273 vaccine on the principle of using mRNA to express protein. mRNA-1273 encrypts the CoV-2 virus glycoprotein along with transmembrane presenter and intact S1 (binding)-S2 (fusion)sites of cleavage. This vaccine has 2 proline substitutions namely for enhancing immune generating capacity at positions 986 and 987 to stabilize the spike protein [45]. Bio stability, was improved when uridine was swapped by N1-methyl-pseudouridine [46]. The mRNA is transported into the humanoid cells by 4 lipid constituting nanoparticle. This nano transporter used in Moderna is ionizable lipid,cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine, and polyethylene glycol-lipid [47,48]. mRNA-1273 prompts potent antibody and T-cell [CD8(+)] response against SARS CoV-2 and protects rodent from infection [45]. The effectiveness of the vaccine was tested in primates (not human) after challenging upper and lower-airway tract with SARS-CoV-2 infection [49]. Vaccination ensued in vigorous virus neutralization

and shielding of the respiratory tracts. It did not cause any pathologic fluctuations or alterations in lungs of tested animals. Trial of (NCT04283461) phase I tested the vaccine with, 45 healthy human adults (18-55) years and 40 more older adults [50,51]. Two doses of were given intramuscular (25/100mg) at an interval of 28 days. Antibodies produced and virus neutralization occurred in ample quantities in both age groups. The phase III trial NCT04470427 tests the vaccine usefulness by inducing 100 g of mRNA-1273 vaccine content in two doses with 28 days gap. Occurrence of COVID-19 was measured after 14 days of the second dose. This trial included 30,000 volunteers, out of which 37%, 42% were of minority community and high-risk category respectively. Pilot data indicated a 94.5% effectiveness against infection with COVID-19 Antagonistic events of local and systemic reactions were spotted [52].

3) United Kingdom / United States of America -Oxford/Astra Zeneca Vaccine

The design for the AZD1222 vaccine was created by the University of Oxford in the UK and Astra Zeneca in Cambridge. This model of vaccine is based on a reproduction deficiency of chimpanzee adenovirus. Viral vectors have been in custom vaccines manufacturing since several decades, characterized by a sturdy CD4+ and CD8+ responses, which makes them a proper vaccine vector for infecting viruses that provoke a strong cellular immune response [53]. Due to the reduced seroprevalence in the human population along with human adenoviruses (Ad5, Ad26), simian adenoviruses are used [54]. AZD1222 is constructed on the platform of ChAdOx1 chimpanzee adenovirus, which carry deletions in the genes E1 and E3 that are anticipated to constrain replication and permitting for the integration of fragments of genetic information. The integrated gene encrypts glycosylated form of the full length spike protein and includes a tissue plasminogen activator as a frontrunner in DNA sequence [55].A phase I/II clinical trial (NCT04324606) with 1077 participants verified that contrary effects of the IM injected vaccine, were fever, headaches and malaise that could be treated with common antipyretic.second immunization was improved by T cell response peak on 14 day and the IgG antibody response at day 28. 91% neutralization response was observed after first immunization and 100% after the second booster.Data from 560 participants phase II/III trial NCT04400838 was published [56]. Adverse effects were similar to the ones reported earlier. In this trial 13 serious antagonist events also occurred, but those were considered unrelated to trial. The responses for binding and neutralization of antibodies were in the appropriate range. The phase III component in this trial tests the vaccine included 12,390 volunteers. The provisional effectiveness analysis of 11,636 volunteers that were enrolled in four trials in South Africa, Brazil, and the UK was published [57] with the efficacy of checking COVID-19 in a test group to be 62.1% after receiving two full doses of the vaccine, nevertheless 90% effectiveness was established in the group receiving a lower first dose followed by second full dose. Overall, the effectiveness was observed to be 70.4%.

4) The Netherlands/United States of America- Janssen Vaccine

The Ad26.COV2.S vaccine was designed and manufactured by the Janssen Vaccines and Prevention BV (Johnson and Johnson). Janssen vaccine is formulated on an adenovirus vector, the

human adenovirus Ad26 [58]. Ad26.COV2.S expresses spike protein, steadied by furin cleavage site mutations and also has two successive proline mutations to stabilize the hinge region. It encompasses the wild-type of signal protein sequence. This vaccine displays powerful neutralizing immunity. Single dose of Janssen vaccine routed via intranasally or intra-tracheally produced binding and neutralizing antibody responses and reduced the occurrence of COVID-19 in species of rhesus macaques [59,60]. Biphase I /II trials were conducted in the US (NCT04436276) and Japan (NCT04509947) to assess safety, reactogenicity, and immunogenicity after IM dose of the vaccine in one or two doses. A phase III trial (NCT04505722) was done on vaccine with 60,000 participants after a single intramuscular dose containing $5X10^{10}$ virus particles. Outcomes measured were occurrence of COVID-19, estimation of viral load, systemic and local reactions, and binding/ neutralizing antibody titres. This experiment was momentarily interrupted because of inexplicable disease in a participant [61]. The III phase trial (NCT04614948) included 30,000 persons leading stress on the molecular confirmation of COVID-19 and co-morbidities.

5) United States of America - Novavax Vaccine

The NVX-CoV2373 vaccine by Novavax (US) is SARS CoV-2 spike protein subunit based vaccine in its glycosylated form [62]. The conformation of this synthetic spike protein is majorly indistinguishable to the natural protein with a minor difference in the S1 subunit and normal alliances between the spike trimers. For escalating immune response, the saponin-centred adjuvant Matrix-Mis was supplemented in the Novavax; spike protein subunit and adjuvant are mixed preceding to inject [63]. NVX-CoV2373 was initially tested on macaque's species that were first vaccinated and then exposed with the native virus challenges [64]. The clinical trial (NCT04368988) was conducted with 131 adult and healthy humans tested the efficacy of two IM injections either with or without adjuvant Matrix-M1. There was interval of 21 days, in 5/25 g dose. Mild fever for one day was observed under adverse reactions. The Matrix-M adjuvant augmented the immune response, and it was quantified by antibody titres and neutralization responses, all of which were compared with quantities estimated from recuperating serum of Covid-2 patient [62]. The phase III trial NCT04611802 in US and mexico was done to testify the worth of the vaccine on volunteers (30,000) in two time doses SARS-CoV-2 rS(5 g) added with Matrix-M1 adjuvant (50g) at 21 days of interval. Side Effects were observed after period 28 - 750 days, which included first PCR-positive test results, and immune responses, inhibition to ACE-2 receptor attachment, and other local adversative effects. Another phase III trial (NCT04583995) in UK tested for the efficacy of the vaccine included 15,000 participants. Observations were outcomes of occurrence of different levels of COVID-19 with its adversities.

6) Russia - Sputnik V Vaccine

The Russian vaccine Sputnik V / Gam-Covid-Vac is structured on the human adenovirus vectors rAd26 and rAd5 combined. Sputnik is manufactured by the Gamaleya National Centre of Epidemiology and Microbiology. Sputnik is heterologous prime booster vaccination to subdue undesirable impacts of the immune response due to the modules of a particular vector exposed [65]. rAd26-S and rAd5-S equally carry full length spike glycoprotein of SARS-covid2 virus. In

phase I trial (NCT04436471) single dose of IM either rAd26-S or rAd5-S was used and resolution of the safety was monitored. In the phase II trial (NCT04437875), the first dose of vaccine was given with rAD26-S, and second dose with rAd5-S as IM shot after interval of 3 weeks. Antagonistic effects were similar as mentioned in all above vaccine trials. Binding and neutralizing antibodies were amplified and the T-cell response increased with CD4+ and CD8+ responses [66]. The (NCT04530396) phase III trial tested vaccine on 40,000 persons with rAd26-S(0.5ml) as first dose and rAd5-S (0.5ml) as second dose. The Epi Vac Corona is another COVID-19 vaccine permitted by Russia, developed by the Vector State Research Centre of Virology and Biotechnology. A single phase I/II trial (NCT04527575) was salvaged for this that started on 26 August.

7) India -Covaxin

Bharat Biotech, India announced analysed data from Phase III clinical trials of Indian vaccine against corona "COVAXIN". It is a whole virion inactivated based vaccine, in collaboration with ICMR and National Institute Virology Pune. It was formulated with a novel chemosorbed imidazoquinolinone (IMDG) on to adjuvant of the aluminium hydroxide gel (Algel+IMDG). IMDG is a Toll-like receptor (TLR)7/8 agonist which has established possibility as vaccine adjuvants, which is known to encourage memory T cell responses along with sturdy neutralizing antibodies. Toll-like receptor can enhance both humoral and cellular immune responses, particularly Th1 responsesas they can directly stimulate Antigen presenting cells(APCs). The activation of cell mediated immune responses is specifically cherished in a multi epitope type (COVAXIN), which achieved immunity enhancing property from S, RBD and N proteins identically. COVAXIN is the first in its kind to authenticate favourable results against asymptomatic infections grounded on qPCR testing and basically help to minmise disease transmission. Mechanism of covaxin has inactivated vaccines which cannot replicate and unlikely to revert to generate pathological effects. They contain dead virus, incapable of infecting people but still have potentcy to instruct the immune system to mount a defensive reaction against it as it would be in actual virus infection. Covaxin along with immune-potentiators, also includes vaccine adjuvants, to boost its immune generating capacity.Covaxin received DCGI approval for Phase I & II Human Clinical Trials in July, 2020. 25,800 volunteers were appointed and randomized in a 1:1 ratio to get the vaccine and placebo. It was randomized, double-blind, placebo-controlled, multicentre phase 3 study. In all trial subjects, more than 2400 volunteers were elders (>60 years) and more than 4500 were with comorbid clinical associations. During trial 130 confirmed cases of covid were found , with 24 were documented in the vaccinated group as opposed to 106 in the placebo receiving group,COVAXIN established 77.8% vaccine worth against symptomatic COVID-19. The vaccine proved its efficacy against severe pandemic disease to be 93.4%. The data establishes 63.6% protection against asymptomatic COVID-19. Safety investigation exhibited adverse outcomes similar to placebo, that came out to be with 12% of volunteers experiencing common side effects and less than 0.5% of volunteers with severe confrontational outcomes [67].

SARSCOV-2 in children and impending benefits of covid-19 vaccines

Children of all ages are vulnerable to SARS-CoV-2 infection and severe disease symptoms. Even though the most of COVID-19 cases in youngsters are asymptomatic or mild, in 0-4 years 18.4/100,000 and in 5–17-year group 10.6/100,000 children require hospitalization. Also, only one-third of total hospitalised cases require intensive care. All ages including infancy and late adolescence, are at risk dynamics for hospitalization. Immunocompromised kids, obesity andunderlying medical comorbidities are potential risk factors for admission to critical care. Multisystem inflammatory syndrome in children (MIS-C) which includes complications myocardial dysfunction, shock, and respiratory failure. Black and Hispanic white children are unduly affected by COVID-19 and MIS-Canalogous to adults. Vaccine against corona possibly could alleviate health inconsistencies among children belonging to ethnic minorities, as has earlier confirmed in other consistently used paediatric vaccines [68].

Table 2: Ongoing clinical trial on vaccines for children age (5-12years)

Company	Location	Estimated number of children	Name	Estimated date of completion	ClinicalTrial ID
BioNTech SE Pfizer	Finland, Poland, Spain, United States	4500	BNT162b2	September 27 2023	NCT04816643
ModernaTX, Inc	United States	13275	mRNA-1273	June 12, 2023	NCT04796896
Bharat Biotech International Limited	India	525	COVAXIN	January 25, 2022	NCT04918797
Sinovac Life Sciences Co., Ltd.	China	12688	Adsorbed COVID-19 (inactivated) Vaccine	February 2022	NCT04456595

Conclusion

Till the present day many vaccines are available, and now vaccines for children have also turned in, but their efficacy and side effects still remain to be unknown as vaccines are composed to be effective for only six-month duration. New variant, Omicron, is emerging as a new threat, and a new question for the current vaccines.

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