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Review Article

Covid -19: A Review on Covid- 19 Vaccines in India

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Abstract:

COVID -19 (corona virus disease 19) or SARS-COV-2 (severe acute respiratory syndrome coronavirus 2) is an emerging infectious disease spreading worldwide. Since there is no medicines discovered against covid -19, vaccines are developed by various manufacturers in a short duration without compromising the safety due to the urgency of vaccines during the pandemic and many vaccines are at the stage of clinical trials. Even though many vaccines are developed, less number of vaccines only got the approval. Various covid 19 vaccines are available in India mainly covishield and covaxin. Vaccination for COVID-19 is very essential as vaccination has proved to decrease severity and prevent mortality due to COVID-19. All people should be vaccinated at the earliest to reduce the impact and severity of covid -19. so, information's regarding covid -19 should be addressed to the public for removing the barriers which prevent them from taking vaccines. Many people are not yet vaccinated due to the misconceptions about vaccines and adverse events following immunization. This article contains a detailed review of vaccines currently available in India.

Keywords: Covid -19, Vaccines, Adverse Events, Covaxin, Covishield, Immunisation

Introduction:

COVID -19 (corona virus disease 19) or SARS-COV-2 (severe acute respiratory syndrome coronavirus 2) is an emerging infectious disease spreading worldwide. Coronaviruses which is a type of beta coronavirus is an "enveloped positive sense RNA viruses" having "spike like projections" on its surface which resembles a crown during microscopic evaluations and so called as coronavirus. The virus spreads by the inhalation of droplets produced during coughing and sneezing by the infected patients or touching the contaminated surfaces by virus and then moving to eyes nose or mouth. Studies suggest that greater viral loads are present in the nasal cavity than in throat. Incubation periods usually varies from 2 to 14 days. Studies identified the entry of virus to the respiratory mucosa is through the angiotensin receptor 2 (ACE2)[1]. The symptoms are sore throat, fever, cough, breathlessness, diarrhoea, nausea and vomiting, headache, fatigue, myalgia. Symptoms may varies person to person[2]. In some patients due to the increased release of inflammatory cytokines like il(2,7,10), G-csf , ip10, mcp1, mip1a, and TNF α disease may progress to pneumonia, respiratory failure or even death. Coronaviruses are mainly divided into four types based on the structural genomics as α, β, γ, and δ. Alpha and beta types only infects mammals. Middle east respiratory syndrome corona virus(mers-cov) and severe acute respiratory syndrome 2(sars-cov2) comes under beta coronaviruses. The coronavirus after infecting the host consist of several steps like attachment, membrane fusion, biosynthesis, maturation and release.

Neurological manifestations of covid-19 in CNS includes encephalopathy, epilepsy, encephalitis, acute myelitis, headaches, dizziness and in PNS hyposmia, neuralgia guillian barre syndrome, dysosmia, dysgeusia are found [3]. Cardiovascular complications are also linked with covid-19 which includes myocardial injury, myocarditis, acute myocardial

infarction, acute heart failure and cardiomyopathy, dysrhythmias, deep vein thrombosis[4]. Hematological complications are lymphopenia, blood hypercoagulability, increased d-dimer levels, prolongation of pt (prothrombin time) and aptt (activate partial thromboplastin time), thrombocytopenia and disseminated intravascular coagulation (dic)[5].Multiple organ dysfunctions is also a complication of SARS COV-2. First step in the pathophysiology includes attachment of virus followed by penetration. Then viral materials will be released inside the host cells and viral RNA goes to the nucleus for replication. Viral proteins are made by viral mrna and the process is called biosynthesis followed by maturation where new viral particles are produced and released. Spike (s), membrane (m), envelop (e), nucleocapsid (n) are the structural proteins of coronaviruses [6]. The receptor for coronavirus was identified to be angiotensin converting enzyme 2 (ACE2) which is mainly found in lungs (lung epithelium), heart, kidney, bladder and ileum [7]. The virus after binding to the host protein, protease cleavage takes place in spike protein by two step sequential process. after undergoing cleavage at s1/s2 cleavage site, spike will be activated which is irrevocable conformational change[8]. The highly pathogenic stage of virus is caused by furin's ubiquitous expression [9]

Diagnosis can be done by real-time reverse-transcriptase-polymerase chain reaction (RRT-PCR) and rapid antigen test using throat swab or nasopharyngeal swab. Other laboratory tests includes WBC count to check lymphopenia, elevated CRP, ESR prothrombin time, creatinine, d-dimer, CPK and LDH. Since there is no approved treatment, preventive measures are taken like wearing face mask and practising hand hygiene with soap or sanitizer [1].

Various covid vaccines are available in india mainly covishield and covaxin. Vaccination for COVID-19 is very essential as vaccination has proved to decrease severity and prevent mortality due to COVID-19. All people should be vaccinated at the earliest to reduce the impact and severity of covid 19. So information's regarding covid 19 should be addressed to the public for removing the barriers which prevent them from taking vaccines. This article contains a detailed evaluation of vaccines currently available in India.

DEVELOPMENT OF COVID -19 VACCINE

When scientists began seeking a vaccine for the SARS-CoV-2 coronavirus in early 2020,they never promised quick success. Previously the fastest vaccine developed was for mumps in 1960, but it was a long period from viral sampling to approval phase , nearly four years . So scientists Expected the vaccine development processes and approval in the year of 2021.But in the month of December, the developer's of several vaccines had announced excellent promising results in large trials. On 2 December, a vaccine made by drug giant Pfizer with German biotech firm BioNTech, became the first fully-tested vaccine to be approved for emergency use. The COVID-19 experience will almost certainly change the future of vaccine science, It revealed how fast vaccine development can proceed when a true global emergency crisis emerges and sufficient resources are available. New ways of manufacturing vaccines, like using messenger RNA (mRNA)and many other clinical trials on vaccines are still ongoing. After the fast manufacturing and approval of covaxin and covishield in India researchers got an idea on how development process can be accelerated substantially without compromising on safety[10].

The researches for developing covid 19 vaccine was not started in the year of 2020 , but for years, researchers was paying attention to related coronaviruses, which cause SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome), and some were working for new kinds of vaccine and their efforts got paid off now spectacularly. Conventional vaccines include viral proteins or disabled forms of the virus itself, which stimulate the body's immune defences against infection by a live virus. But the first two COVID-19 vaccines for which efficacy was reported in large-scale (phase III) clinical trials used a string of mRNA inside a lipid coat. The mRNA encodes a key protein of SARS-CoV-2; our body produce this protein once mRNA get inside our cells which will acts as the antigen. The vaccines made by Pfizer and BioNTech and by the US pharmaceutical company Moderna both use mRNA that encodes the spike protein, which docks to human cell membranes and allows the coronavirus to invade the cell. A lot went into the

mRNA platform that we have now. The basic research on DNA vaccines started before 25 years ago, and RNA vaccines have been benefited from 10–15 years of strong research. The approach has matured just at the right time.[10]

COVID VACCINES IN INDIA

As covid vaccination programme has started in India, many people are nervous about whether to take vaccine or not due to their concerns about ADR. Currently mRNA vaccine, viral vector vaccine, protein subunit vaccine are the three types of vaccine which are developed and studied in clinical trials. [11]

Vaccination against COVID-19 commenced in India on January 16, 2021. the government is compulsing all citizens to get immunized at the earliest. currently in India there are eight COVID-19 vaccines under investigation at various phases of clinical trials. Among them four were developed inside the country. The government approved the use of Oxford-AstraZeneca vaccine which is named as covishied in India and Covaxin, which is manufactured by Bharat Biotech. In the initial stage about 30 million healthcare workers were vaccinated [12]. The Indian government implemented urgent measures to enlarge the country's vaccine production capacity and later on developed an effective digital system to address and evaluate all the aspects of vaccine administration [13].

MECHANISM OF VACCINES

These vaccines contain instructions for antigens that stimulate the body's immune system to produce antibodies against theSARS-CoV-2 proteins. mRNA vaccines will provide cellular material, leads to the production of SARS-CoV-2 proteins which further stimulate the T and B lymphocytes production. mechanism of vector vaccines is exposing the body to a weaker version of a live virus containing SARS-CoV-2genetic material, hence called as viral vector. It further advances protein production and the body will make copies of these proteins and stimulates production of T and B lymphocytes. In Protein subunit vaccines pieces of proteins which cause SARS-CoV-2 infection are injected. Those proteins are identified as foreign and stimulate the release of T lymphocytes. For all of the above vaccine types, antibodies against SARS-CoV-2 proteins will be circulated in body following vaccination and helps to fight against future infection [11].

CoWIN (Covid Vaccine Intelligence Work)

Co WIN is a web portal of Indian government created for covid-19 vaccine registration. It is completely owned and operated by Ministry of Health and Family Welfare of India. It exhibit booking slots of vaccine available in nearby areas and can be booked using the website. The certificate after COVID-19 vaccination can also be obtained through the platform [14]

Table 1: Potential vaccine candidates in India

Company and collaborating agency	Brand name	Vaccine type	Storage temperature
Serum Institute of India (SII), Pune, India (in collaboration with the University of Oxford, UK, and pharma giant AstraZeneca)	Covishield	Non-replicating chimpanzee adenovirus vaccine vector (ChAdOx1)	2–8 °C
Bharat Biotech Ltd, Hyderabad, India (in collaboration with the National Institute of Virology of ICMR, India)	Covaxin	Inactivated-virus vaccine	2–8 °C
Cadila Healthcare, /Zydus Cadila, Ahmedabad, India (supported by the Department of Biotechnology, Government of India)	ZyCoV-D	Plasmid DNA vaccine	2–8 °C
Dr. Reddy's Laboratories, Hyderabad, India (vaccine developed by Gamaleya National Research Institute of Epidemiology and Microbiology, Moscow, Russia)	Sputnik V	Inactivated human adenovirus Ad5 and Ad26 with Spike proteins inserts	−18 °C*
Gennova Biopharmaceuticals Ltd, Pune, India (in collaboration with HDT Biotech Corporation, USA)	HDT-301	mRNA vaccine	2–8 °C

COVISHIELD (SERUM INSTITUTE OF INDIA)

Serum Institute of India (SII), Pune, has signed agreements with Oxford-AstraZeneca in vaccine production which is now producing at a large scale, the Oxford- AstraZeneca Adenovirus vector-based vaccine AZD1222 is named as "Covishield" in India. and it has stocked about 50 million doses in the initial stage and produced more doses later on accordingly [15]. Covishield is produced under the "at-risk manufacturing and stockpiling license" from the Drugs Controller General of India (DCGI), and the Indian Council for Medical Research (ICMR). The ICMR provided the fund for the clinical trials of the Covishield vaccine.

The Serum institute of India and ICMR combined together and conducted Phase II/III, observer- blind, randomized, controlled study in some of the healthy adults at 14 centers allover India for comparing of the safety of Covishield (manufactured in India) and original Oxford-ChAdOx1 in the prevention of COVID-19 disease. The efficacy was found to be 70.42%. The safety and immunogenicity data obtained from the clinical trial in India was comparable with the data from previous trials done outside of India [16].

ADVERSE EVENTS FOLLOWING FIRST DOSE OF COVISHIELD

The common Minor AEFIs reported are Pain at the injection site in Fever ,Myalgia, Lethargy and Headache . studies showed that 92.45% and 86.79% of subjects experienced AEFI with COVISHIELD's 1st dose and 2nd dose respectively. In a study 2 cases showed serious AEFI. first case showed abdominal cramps and episodes of loose stool in first one hour of vaccination and later on syncopal attack along with significant postural drop in blood pressure and chest tightness without wheeze. The patient treated with intramuscular Adrenaline 0.5 mg (1:1000) and patient was symptomatically better and discharged .but again she was admitted with recurrent episodes of syncope along with significant postural drop in blood pressure. Again she was treated with intramuscular Adrenaline . Patient also complained about dizziness and chest tightness on exertion and it gradually decreased after 24 hours and shown improvement after applying 'deep venous thrombosis(DVT) stocking' while standing and walking [17] .

Second case was also having same complaints like abdominal cramps and postural drop within 6 hours post vaccination. the patient was treated with intramuscular adrenaline and discharged when patient got symptomatically stable. Third case is a patient with Severe Minor AEFI after vaccination. The patient presented with urticaria and an episode of syncope in the first 24 hours after vaccination. Patient was treated with one dose of Intramuscular Adrenaline and later on got discharged since she was symptomatically better and no follow up was required. The possibility of some laboratory abnormalities following the adenovirus-based COVID-19 vaccine, like transient neutropenia and lymphopenia fasting hyperglycemia, have been listed. [17,19]

Incidence of Minor AEFIs after COVISHIELD (COVID-19) vaccine

Very common AEFIs

- Pain at injection site
- Fever
- Myalgia
- Lethargy
- Headache
- Chills
- Rigor

Common AEFIs

- Joint pain
- Nausea
- Vomiting
- Sweating
- Running nose
- Swelling at injection site Diarrhoea
- Cough
- Redness at injection site
- Loss of Appetite
- Dizziness

Uncommon AEFIs

- Sore throat
- Abdominal pain
- Skin rashes
- Itching
- Shortness of breath
- Palpitation

- Syncope
- Chest tightness

The reason for hypoperfusion(after vaccination is due to the release of cytokines like IL4, IL17 mediating proinflammatory function, and release of interferon-gamma activating inducible nitric oxide synthase (iNOS) responsible for the vasodilatory effect [18] . The symptom onset was within the first two hours of vaccination and had a biphasic course. The onset of anaphylaxis can occur after several minutes but rarely up to two hours of vaccination. Biphasic reactions where symptoms recur 8-12 hours after onset of the original attack, and prolonged attacks lasting up to 48 hours, have been described. The symptom occurred within the first two hours of vaccination and had a biphasic course. Anaphylaxis may occur after several minutes but rarely occurs after two hours of vaccination. Biphasic reactions are symptoms that reoccur after 8-12 hours following the onset of the original attack, and prolonged attacks which may last up to 48 hours. [20,21]

Reports suggested there is no causally related Serious Adverse Events due to the study vaccine has been found . However, a specific form of severe cerebral venous thrombosis associated with thrombocytopenia and bleeding has been reported in seven cases who were vaccinated with COVID-19 [20-22]

COVAXIN

Covaxin was developed by Indian pharmaceutical company Bharat Biotech in collaboration with the Indian Council of Medical Research, a government funded biomedical research institute, and its subsidiary the National Institute of Virology. Bharat Biotech has brought to market 16 original vaccines, including for rotavirus, hepatitis B, Zika virus, and chikungunya.[23,24]

MECHANISM OF ACTION

It uses a complete infective SARS-CoV-2 viral particle consisting of RNA surrounded by a protein shell, but modified so that it cannot replicate. Covaxin comes as a two-dose regimen, recommended to be taken 84 days apart.[25]

APPROVAL OF COVAXIN

The Central Drugs and Standards Committee (CDSCO), India's top drug regulator, issued an emergency approval for Covaxin on 3 January 2021, even though phase III clinical trials are still ongoing and phase II studies are unpublished.14 The regulator cited the need for protection against the potential spread of the UK variant. No peer reviewed evidence is available to show that the vaccine would be effective against this strain, although a preprint indicates promising results.15 The vaccine is currently being administered in India to people over 60 and those over 45 with comorbidities, as well as to health workers. [26,27]

ADR OF COVAXIN [28,29,30]

Mild Reactions:

- Injection site pain
- Fatigue
- Headache
- Myalgia
- Pyrexia
- Chills
- Arthralgia
- cold extremities

Severe Reactions:

- Hypotension
- Anaphylaxis

Studies showed that 77.27% and 72.72% of subjects have experienced AEFI with COVISHIELD's 1st dose and 2nd dose respectively. there were no potential thromboembolic events reported following e Covaxin vaccine administration.[31] The important abnormal laboratory parameters after vaccination included derangements in bilirubin, SGOT, SGPT, Cholesterol C-reactive protein levels. These findings had no corroborating clinical manifestations. There was one serious adverse event reported in a study group due to which the patient was hospitalized. Five days post-vaccination the participant tested positive for SARS-CoV-2 and the symptoms included fever and headache. This event was not causally associated with the vaccine .[32]

VIGIBASE

VigiBase , an international pharmacovigilance post-marketing database of the World Health Organization(WHO), which includes all adverse

events of drugs reported across worldwide.[33] Literature proves that VigiBase was previously used to analyse the adverse events related to several repurposed drugs for COVID-19.[34-37] In the absence of definite post-vaccination robust data on adverse events related to the COVID-19 vaccines, most of the studies conducted on COVID-19 vaccines are based on the data generated from these vaccines' clinical trials and on the data available in the VigiBase.[38-40] Since all COVID-19 vaccines are new drugs; it is mandatory to monitor their adverse events post-approval.

VACCINE-VIGILANCE IN INDIA

In India, we have AEFI Program. The Immunization Division of MoHFW (Ministry of Health & Family Welfare) has taken few steps to strengthen the national AEFI surveillance system for COVID-19 vaccinations. They have National AEFI Committee which closely monitors the Non-Serious/ Serious adverse events reported with the COVID-19 vaccine. The causality assessment is done by a Special Group of Experienced Physicians and Health care workers. The data gets published on the portal of MoHFW on monthly basis for public interests. Not always all the reported cases have a causal relationship with the drug, hence the Causality assessment and identifying the right safety information is very important (AEFI Guidelines MoHFW, 2021). Despite Govt. awareness campaign at vaccination centres in India for AEFI Reporting, AEFI cases are still underreported. People need to understand the importance of AEFI Cases [(31)].

CONCLUSION

Vaccination for COVID-19 is very essential as vaccination has proved to decrease severity and prevent mortality due to COVID-19. Both the vaccines (covaxin and covishield) are equally efficacious in terms of the prevention of the COVID-19 disease and decreasing the severity of the COVID-19 Infection and also it is safe to use. Risk-Benefit ratio of both the vaccines is balanced. Vaccine-vigilance surely play a very climacteric role in the future. The Indian government implemented urgent measures to enlarge the country's vaccine production capacity and later on developed an effective digital system to address and evaluate all the aspects of vaccine administration. To boost the confidence in public, the Govt. officials such as Ministers, CMs, PM, and healthcare workers took the vaccine first in India. Likewise all people should be vaccinated at the earliest to reduce the impact and severity of covid 19. Many people are not yet vaccinated due to the misconceptions about vaccines and adverse events following immunization. More vaccination awareness should be addressed to the public because many people are not yet vaccinated due to the dilemma in various aspects of covid vaccines .

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