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Covid-19 Vaccines are Not 100% Productive and Their Global Controversies

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Abstract

Coronavirus disease 2019 (COVID-19), continuous to be challenging for all the scientist and healthcare professionals all over the world. They are in search of a solution that either prevents the infection or to avoid the spreading of the disease as of now in the global pandemic situation. However, scientists and virologists working together to find out the cure for infection. And to prevent of spreading infection before it becomes complicated among the public, we have vaccines to keep lives preventive from the deadly virus however the controversies and hesitancy for the vaccines also precisely increased day by day among the social network and the laypeople by spreading incorrect information about the vaccination and immunization. To ensure the vaccines are safe and the immunization helps people who are recovered from the infection and yet to be infected, herein we discuss the covid 19 vaccine and their efficacy. The questions underlying the type of immune response they may elicit, the consequences that new mutations may have in the generation of sub-strains of SARS-CoV-2 and their impact and challenges for the efficacy of potential vaccines in a scenario post-pandemic.

Keywords
Covid-19, Covaxin, Sputnik-B, Covishield, Vaccine.

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INTRODUCTION:

The SARS-CoV-2 coronavirus, the etiologic agent of COVID-19 has been so far responsible for more than 18.2cr cases and nearly 39.5L deaths worldwide. The etiological agent which causes Respiratory tract infection (RTI). That can range from mild to lethal. The mild illness causes the common cold while more lethal varieties can cause SARS, MERS, and COVID-19. Coronavirus is Zoonotic, which means that the virus is transmitted between animals and humans. It has been determined that MERS-CoV-2 was transmitted from animals to humans. The source of the covid 19 is yet to be determined, but investigations are ongoing to identify the Zoonotic source to the outbreak[1].

The virus may cause respiratory failure in such a way that all the clinical presentation and morbidity is high even people cannot tolerate the symptomatic representations and comorbid diseases in geriatrics and adults. The lungs are the organs most affected by the virus because the virus accesses host cells via the receptor for the enzymes angiotensin-converting enzyme 2(ACE2), which is more abundant on the surface of type 2 alveolar cells of the lungs the virus uses a special surface glycoprotein called a "spike" (peplomer) to connect the ACE 2 receptor and enter the host cell.

The least victim of SARS-CoV-2 infection is the (LRT) lower respiratory tract. Which is causing flu-like illness with symptoms such as cough, fever, fatigue and arthralgia. However, the presentation and the

course of the disease can range from asymptomatic to mild respiratory infections and pneumonia. Some infected patients develop more severe disease with acute respiratory syndrome distress (ARD) about 7–10 days after onset of symptoms, following a rapid viral replication, increased pro-inflammatory cytokine production, "cytokine storm", as well as chemokine responses and inflammatory cell infiltrates[2].

Among other risk factors identified, age has shown to be an important factor for the development of more severe diseases. Younger individuals often are asymptomatic or present mild symptoms and thus might have a crucial role in the spread of the disease. During viral infection, both innate and adaptive immune responses play a role in the pathogenesis of SARS-CoV-2. Specific motifs present in some SARS-CoV-2 protein structure or mediators released by infected damaged cells are recognized by the conserved innate pattern recognition receptors (PRRs) and seems to be involved in the modulation of the immune response.

Important note the pathophysiology of SARS-CoV-2 is the overproduction of early pro-inflammatory cytokines such as tumour necrosis factor (TNF), IL-6 and IL-1β which may lead to increased risk of vascular hyper permeability, multi-organ failure and eventually death if the high concentrations of cytokines are not controlled. Moreover, it has been observed that adults with COVID-19 often present a decrease in both CD4+ and CD8 + T-cell subsets at the early stage of the disease that would contribute to virus replication and disease severity in some patients.

Innate immunity is important to inhibit viral replication and clearance, as well as to induce tissue repair and prolonged immune response. In this context, type I interferons (IFN-I, IFNα, IFNβ) play an important role in conferring antiviral activity in host cells. However, it seems that SARS-CoV-2 have evolved mechanisms to evade IFN antiviral activity. Nevertheless, given the complexity of COVID-19 pathophysiology, type I interferons may have different roles at different stages of infection or mild versus severe COVID-19 patients. Despite these findings, the immunity profile in COVID-19 is not completely understood[3].

VACCINE AND ITS IMPORTANCE:

Even before COVID-19 was declared a pandemic on March 11th, 2020; efforts trying to develop a vaccine against SARS-CoV-2 had been initiated, when the first viral genomic sequence became available in early January. However, the recognition of the pandemic intensified and induced a rush for the development of vaccines in different countries. Thus, considering the rapid global spread of SARS-CoV-2 infection and the increasing death toll, the development of an effective vaccine became the priority. As result, great advances in a shorter time than expected for this research field was conquered, and several vaccine candidates are currently in phase II/III in China, UK, the USA, Russia, Brazil and other countries.

Vaccines have played an important role in public health for decades to help prevent diseases like mumps, polio, rubella and yellow fever. Yet, we still have not understood well about their durability. Several questions have been raised regarding the novel vaccines being developed for SARS-CoV-2, especially concerned with efficacy and durability. This review will highlight important structure-function relationships of key SARS-CoV-2 proteins with a focus on their role in pathogenesis and ability to elicit immune responses. We also will discuss the impact of new mutations in the genome of SARS-CoV-2 and how these changes can contribute to the emergence of new sub-strains with novel fitness and transmissibility ability, which could circumvent the efficacy and durability of the vaccines under development[4,5].

SARS-COV-2 TARGET PROTEINS AND STRATEGIES FOR VACCINE DEVELOPMENT:

Structural proteins that are exposed at the virus surface are more likely targets for a vaccination approach. These include the envelope spike protein S, the small envelope protein E, the matrix protein M and the nucleobase protein N, although the latter is unexposed at the surface. The spike S protein is a glycoprotein composed of 1273 amino acids with three subunits S1, S2 e S2' and is the major component of the SARS-CoV-2 envelope.

It is essential for host receptor binding and virus entry, and among the other viral proteins is the main focus of vaccine development. The three subunits of S protein act differently during the process of binding to the host cell receptor ACE2 and undergo conformational changes induced upon its entry into the endosomes of the host cell. S1and S2 subunits form functional prefusion trimers after proteolytic cleavage. The RBD region of the S1 domain undergoes a hinge-like conformational movement, which is an important determinant of host cell receptor binding. Interestingly, SARS-CoV-2 S protein has a 4 amino acid insertion (PRRA) in the S1/S2 cleavage site which is different from SARS-CoV.

This insertion results in a polybasic RRAAR Furin-like cleavage motif that enhances infection in lung cells. This demonstrates that the RBD region in the S protein is the most variable part of the SARS-CoV-2

and has implications with the virus pathogenesis. Potential targets for a putative SARS-CoV-2 vaccine were identified based on previous immunological studies performed with the beta coronavirus SARS-CoV. In one study, a set of B- and T-cells epitopes derived from the spike and nucleocapsid proteins that map identically to SARS-CoV-2 proteins were identified. The screening of these epitopes took into consideration only one hundred twenty SARS-CoV-2 genomic sequences available at the beginning of the COVID-19 pandemic (Feb 2020), and no mutations were observed in these epitopes at that time.

A population coverage analysis of the associated MHC alleles was performed and based on that; it was proposed an estimated set of epitopes that could provide broad coverage. It seems that the entire RBD region remains conserved in SARS-CoV-2 isolates, and some rare non-synonymous mutations in the S protein have been described V483A, L455I, F456 V and G476S. However, as new genomic sequences are known novel mutations may be revealed that could impact the pathogenicity of SARS-CoV-2.

As of December 7th, 2020, there were more than 245,000 genomic sequences available from SARS-CoV-2 isolated from different countries at different times since December 2019, according to the Global Initiative on Sharing All Influenza data. Therefore, it would be important to keep the analysis of SARS-CoV-2 genomes to identify and determine the potential biological effects of novel mutations in the epitopes identified preliminarily[6,7].

VACCINES AVAILABLE IN THE MARKET:

There are very few numbers of vaccines available in the market and has efficacy to fight against covid 19 .as of we have Pfizer, Moderna and Johnson and Johnson's and biotech and Gamaleya these are the companies and the research find the solution to prevent from the infection and therefore to save lives they fight against the mRNA virus and also need the booster dose to improve the efficacy[8]. They are

- COVAXIN
- SPUTNIK-B
- COVISHIELD
- MODERNA COVID VACCINE

COVAXIN

The India's first indigenous covid 19 vaccine, by Bharat biotech in collaboration with the Indian council of medical research (ICMR). It is also called a whole virus vaccine. The clinical name of the vaccine BBV152 which is an inactivated type. The route of administration of the vaccine is an intramuscular injection. So far it has shown 78% efficacy according to phase 3 clinical data. The indigenous inactivated vaccine is developed BSL-3(BIOSAFETY LEVEL 3). It has been developed with the whole Viron inactivated Vero cell (platform technology). [inactivated Viro cell designed platform technology]. Inactivated vaccines do not replicate and are therefore unlikely to revert and cause pathological effects.

They contain dead viruses, incapable of infecting people but still able to trigger the /instruct the immune system to mount a defence reaction against infection. the vaccines phase 1 and phase 2 clinical trial data states that other reported adverse events include

- Fatigue
- Body aches
- Nausea
- Vomiting
- And chills

No sessions of side effects are reported.

MOHFW-suggests to alleviate some mild effects. They suggest paracetamol with a dose of 500 –650 mg (acetaminophen, tyelol). Allergies and contraindications are very rare.

Symptomatic representations such as

- Difficulty in breathing
- Swelling of face and throat
- A rapid heartbeat
- Rashes throughout the body and
- Dizziness
- Weakness

Major Contraindication is seen with people who is prone to allergies[9,10].

CONTROVERSIES ABOUT APPROVALS

All India people's science network states that the intense concerns arising from the absence of efficacy data. The new Indian express states that irresponsible statements of vested interests are politically driven and harming the credibility of the research. Expert reports- states that this vaccine is a whole virus inactivated vaccine which may provide better protection even against mutant strains of the virus as the immune response will be against multiple antigens and not only against spike protein.

SPUTNIK-B

Sputnik B is a vaccine which is developed by the Gamaleya research institute. Gam -covid –vac is the research name. type of this vaccine is quite specific which is a non-replicating viral vector and the route of administrations is an intramuscular injection.

Sputnik B is widely used in Russia. approved and used in over 60 countries. The review of the vaccine is undergoing by WHO and European medical agency (EMA).

WHO review was carried out between MAY 31 and June 4 2021. In its statement, the pharma standard listed the concerns as well as the action taken in response.

The Gamaleya institute subsequently reported an impressive efficacy rate of 92% based on early analysis of phase 3 data, close to the 95% rate reported by Pfizer/Biotech and 94.5% rate reported by Moderna. there are common side effects reported in clinical trials as well as controversies around potential safety concerns of the vaccines .it is the 1st covid 19 vaccine in the world to be authorized for use against the SARS-COV2 virus.

Sputnik-B is a two-part adenovirus viral vector vaccine with an efficacy rate of 91.6%.

Adenovirus is the type of virus associated with the common cold and other illnesses. They seem as a delivery vehicle for the DNA instructions to produce Spike protein of the SARS –COV-2 virus in the body. This triggers the production of antibodies against this spike protein, preparing the immune system for a potential infection.

Each dose uses a different type of adenovirus. 1st dose with type 26(Ad26). A booster dose with type –5(ad5). The purpose of using two different types is to lower the possibility of the body developing antibodies against adenovirus, after the first dose, which could make the second dose ineffective[11].

COMMON SIDE EFFECTS

An infection analysis of phase 3 clinical trials in Feb 2021. Reports on the efficacy and safety of the vaccine, based on the data, the most common side effects were.

- Flu-like illness
- Headache
- Fatigue
- Injection site swelling /site reaction

Are most commonly similar to other vaccines are noted by the centres for disease control and prevention (CDC).

COVISHIELD-COVID 19 VACCINE

COVISHIELD vaccine is developed by AstraZeneca, Serum Institute of India. AZD1222(chad0x1) is the research name. The type of the vaccine is non-Replicating viral vector and administered by intramuscular injection. Also known as Oxford, AstraZeneca vaccine, and the total number of doses are 2. the vaccine has 70% efficacy seen in patients after its two doses.it is approved by the health department, Govt of India. covid vaccine efficacy rate after 2nd dose is considered to be around 90%.

The most common side-effects are from the clinical data

- Swelling
- Heat
- Tenderness
- Itching
- Pain, redness is visible only at the injection site.

Common cause itching, mild body ache, cold and tiredness.

According to the central drug standard organisation (CDSCO). 2 doses have approved the timeline between 2 doses are 4-6 weeks[12].

MODERNA'S COVID 19 VACCINES

Approved by the U.S food and drug administration (FDA). For EUA then it may be made available without post-approval bridging trials and the testing of every batch of the waxing by central drug laboratory.

DCGI grants emergency use approval for a ready-to-use lab.

DRUGS CONTROLLER CENTRE OF INDIA (DCGI). On 29th June 2021, granted permission to Mumbai based pharma major Cipla to Imports Moderna's covid 19, making it the fourth vaccine in the country to be given in the emergency use authorization EUA. Moderna's vaccines can be stored for a period of 7 months at a prescribed temperature. And normal storage after the vial is opened is 30 days. It has shown to have an efficacy of approved 94% protection against covid 19 starting 14 days after the first dose.0.20mg/ml it is an mRNA vaccine to be developed so fae .it has a multiple-dose vial. (Based on the evidence collected so far, the new varieties of SARS-COV-2 do not matter the effectiveness of vaccine).

HOW TO OVERCOME VACCINE HESITANCY AND MISINFORMATION:

Health care professionals play a central role in confidence in vaccines and their recommendations are strong driven off vaccine acceptance among laypeople. In many countries, however, a considerable production of these professionals is affected by vaccine hesitancy which in turn may be fostered by a lack of tests in health authorities. Most healthcare professionals are not experts in vaccination they may share with laypeople uncertainties about the benefits and safety of vaccines and attitudes of banalization of certain. vaccine-preventable disease. This may negatively affect their uptake of vaccines that are recommended to protect their patients and themselves such as seasonal influenza vaccination.

This may also well promote vaccine hesitancy among their patient's hesitancy. Healthcare professionals may not address their concern regarding vaccine approximate appropriately. Nonetheless, because those uncertainties diminish as their medical education level increase is a major investment in the initial training of healthcare professionals in the area of vaccination is necessary. Trust in the healthcare system the expert defining vaccinations strategies

and more generally in government bodies also affect vaccine acceptance.

Vaccine hesitancy is also associated with the structural crisis of confidence in science and technology, this enchantment with science results from the balkanization of scientific knowledge that is the dissemination of multiple results and knowledge all increasingly partial, confidential, professional, and even contradictory.

This scientific knowledge produced since the beginning of the COVID-19 patient pandemic has not except escaped this balkanization magnified by new information and communication technology to use vaccine we are constrained to trust them.

This leap of faith conceptualised by sociologist Anthony Giddens as "reluctant trust is required not only for laypeople but also for health care professionals".

This reductant trust can be explained why people accept or recommend a vaccine even as they are so uncertain about its benefits and risks, this related trust has become structural and fragile and has barely been assessed in the survey of vaccine hesitancy.

Finally, exposure to criticism of vaccination misinformation and "anti-vax" activists of them through social networks and the Internet plays a major role in the crisis of trust in vaccination paradoxically individual distrust the source of information but exposed to its content can induce emotions and slow doubt occurrence to conspiracy theories, which are recent studies in England found among almost half of the population a prior promote mistrust against future covid- 19 vaccines[13,14,15].

CONCLUSION:

In conclusion, identifying effective approaches at the individual and social levels to restore trust in vaccination is an essential issue that must be prioritised by researchers together with share measurements tools and methodology guidance to facilitate the sharing of knowledge.

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