Covid-19 Variants and Vaccines: An Overview

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Introduction

Coronavirus disease 2019 (COVID-19) is the highly contagious viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and Middle Eastern Respiratory Syndrome (MERS) appeared in Wuhan, Hubei Province, China, in late December 2019. COVID-19 considered as worldwide pandemic because of their rapid prevalence in whole world and their catastrophic impact on various disciplines such as economy, industry, education, etc. (Marco Cascella, 2021). Moreover, according to World Health Organization (WHO), COVID-19 takes life of more than 4.47 million people and it would destroy the livelihoods people health systems because it is spread through close contact with infected people and could also be transmitted by asymptomatic patients (kern, 2021).

The most characteristics of the COVID-19 are Fever, Dry cough, Fatigue. However, there are other less common symptoms such as Loss of taste or smell, Nasal congestion, Conjunctivitis (also known as red eyes), Sore throat, Headache, Muscle or joint pain, Different types of skin rash, Nausea or vomiting, Diarrhea, Chills or dizziness (Maladie à coronavirus (COVID-19) : Symptômes et traitement, 2021).

Since SARS-CoV-2 affected the Ribonucleic (RNA) and deoxyribonucleic acids (DNA), Reverse Transmission Polymerase Chain Reaction (RT- PCR) was the gold standard method for diagnosing Covid-19 (Alazab, 2020). RT-PCR tests are performed on clinical research samples of nasal secretions by inserting a swab into the nostril and gently moving it into the nasopharynx to collect secretions (Alazab, 2020). Meanwhile, some patients get negative tests even though they had abnormality in their chest radiography.

Chest radiography has great results for important clinical findings such as computed tomography (CT) scans and X-rays images. They frequently used for diagnosing Pneumonia and other chest diseases. Due to their great impact in the medical care worldwide, CT scans and X-rays were highly recommended for the detection of Covid-19 (Jain, 2020).

1. Covid-19 Variants of Concern (VOCs)

As SARS-CoV-2 is RNA virus, it has the ability of genetic evolution with the development of mutations over time, what create new variants with different characteristics. According to WHO, four concern variants (VOC) were discovered (Marco Cascella, 2021):

The first variant of the virus was in December 2020 in United Kingdom (UK) called Alpha (B.1.1.7). In the same period other two variants called Gamma (P.1 lineage) and Delta (B.1.617.2) in Brazil and India respectively. While Beta (B.1.351) variant was discovered South Africa.

1.1 Alpha (B.1.1.7 lineage)

Alpha variant also known as GRY (formerly GR/501Y.V1) is new SARS-CoV-2 variant caused by 17 mutations in the viral genome. Eight mutations (Δ69-70 deletion, Δ144 deletion, N501Y, A570D, P681H, T716I, S982A, D1118H) are in the spike (S) protein. N501Y shows an increased affinity of the spike protein to ACE 2 receptors, enhancing the viral attachment and subsequent entry into host cells. The UK variant was the most contagious one with 43% to 82% times than the original SARS-CoV-2. The clinical study reported that the B.1.1.7 lineage variant had increased severity of disease compared to patients that had other variants of SARS-CoV-2.

A lot of study were done in UK confirmed that the mortality risk of infected patients with this variant was 1.64 (95% confidence interval 1.32 to 2.04, $P<0.0001$) patients with previously circulating strains.

Another study reported that the B 1.1.7 variant was associated with increased mortality compared to other SARS-CoV-2 variants (HR= 1.61, 95% CI 1.42-1.82) (Davies, 2021). The risk of death was reportedly greater (adjusted hazard ratio 1.67, 95% CI 1.34-2.09) among individuals with confirmed B.1.1.7 variant of concern compared with individuals with non-1.1.7 SARS-CoV-2 (Grint, 2021).

1.2 Beta (B.1.351 lineage)

Beta variant also known as GH501Y.V2 is another variant appeared South Africa in October 2020. GH501Y.V2 has nine mutations (L18F, D80A, D215G, R246I, K417N, E484K, N501Y, D614G, and A701V) in the spike protein, of which three mutations (K417N, E484K, and N501Y) are located in the RBD and increase the binding (K417N, E484K, and N501Y) are located in the RBD and increase the binding affinity for the ACE receptors.

1.3 Gamma (P.1 lineage)

Gamma variant or GR/501Y.V3 was detected in Brazil in December 2020. The variant has ten mutations in the spike protein (L18F, T20N, P26S, D138Y, R190S, H655Y, T1027I V1176, K417T, E484K, and N501Y). Three mutations (L18F, K417N, E484K) are located in the RBD, similar to the B.1.351 variant (Faria, 2021).

1.4 Delta (B.1.617.2 lineage)

As December 2020, India identified the B.1.617.2 as new variant of SARS-CoV-2. Also, Delta variant has ten mutations (T19R, (G142D*), 156del, 157del, R158G, L452R, T478K, D614G, P681R, D950N) in the spike protein. Nowadays, B.1.617.2 variant is the most dominant SARS-CoV-2 strains in the world wide.

2. Covid-19 Variants of Interest (VOIs)

By June 22, 2021, The WHO defines some variants that have remarkable specific genetic which might accelerate the transmission of the virus and even more reduce the natural immune response of the body and decrease in the effectiveness of therapeutics or vaccination. The VOIs declared by WHO are: Epsilon (B.1.427 and B.1.429); Zeta (P.2); Eta (B.1.525); Theta (P.3); Iota (B.1.526); Kappa (B.1.617.1) and Lambda (C.37).

2.1 Epsilon (B.1.427 and B.1.429)

Epsilon (B.1.427 and B.1.429) variants, also called CAL.20C/L452R, emerged in the US around June 2020 and increased from 0% to >50% of sequenced cases from September 1, 2020, to January 29, 2021, exhibiting an 18.6-24% increase in transmissibility relative to wild-type circulating strains. These variants harbor specific mutations (B.1.427: L452R, D614G; B.1.429: S13I, W152C, L452R, D614G) (Zhang, 2021).

2.2 Zeta (P.2)

Zeta (P.2) has key spike mutations (L18F; T20N; P26S; F157L; E484K; D614G; S929I; and V1176F) and was first detected in Brazil in April 2020.This variant classified as a VOI by the WHO and the Centers for Disease Control and Prevention CDC due to its potential reduction in neutralization by antibody treatments and vaccine sera.

2.3 Eta (B.1.525) and Iota (B.1.526)

Eta (B.1.525) and Iota (B.1.526) variants harbor key spike mutations (B.1.525: A67V, Δ69/70, Δ144, E484K, D614G, Q677H, F888L; B.1.526: (L5F*), T95I, D253G, (S477N*), (E484K*), D614G, (A701V*)) and were first detected in New York in November 2020 and classified as a variant of interest by CDC and the WHO due to their

potential reduction in neutralization by antibody treatments and vaccine sera.

2.4 Theta (P.3)

Theta (P.3) variant, also called GR/1092K.V1 carry key spike mutations (141-143 deletion E484K; N501Y; and P681H) and was first detected in the Philippines and Japan in February 2021 and is classified as a variant of interest by the WHO.

2.5 Kappa (B.1.617.1)

Kappa (B.1.617.1) variant harbor key mutations ((T95I), G142D, E154K, L452R, E484Q, D614G, P681R, and Q1071H) and was first detected in India in December 2021 and is classified as a variant of interest by the WHO and the CDC.

2.6 Lambda (C.37)

Lambda (C.37) variant was first detected in Peru and has been designated as a VOI by the WHO in June 2021 due to a heightened presence of this variant in the South American region.

3. Covid-19 Transmission

As SARS-CoV-2 is respiratory virus, it is obvious that the first way of their transmission is the close contact with infected people. Also, contact with surfaces contaminated by the virus, airborne transmission with aerosol-generating procedures and fomite transmission from contamination of inanimate surfaces with SARS-CoV-2 could be source of infection.

Researchers reported that SARS-CoV-2 can be found on plastic and stainless steel for up to 2-3 days, cardboard for up to 1 day, copper for up to 4 hours. Moreover, it seems that contamination was higher in intensive care units (ICUs) than in general wards, and SARS-CoV-2 can be found on floors, computer mice, trash cans, and sickbed handrails as well as in the air up to 4 meters from patients implicating nosocomial transmission as well in addition to fomite transmission (Guo, 2020).

4. The Main Types of Covid-19 Vaccine

Since the declaration of Covid-19 as worldwide pandemic by WHO, experts from various organizations started searching for an accurate vaccine for this pandemic. Till now, various types of vaccine authorized by the WHO: Whole Virus, Protein Subunit, Viral Vector and Nucleic Acid (RNA AND DNA). All vaccines work by exposing the body to molecules from the target pathogen to trigger an immune response with different exposure method.

The main objective of these categories is to get immunity to the virus, and stop the

transmission by smuggling the antigen into the body, or by using the body's own cells to make the viral antigen (Gavi, 2021).

A. Whole Virus

Whole virus vaccines use a weakened (attenuated) or deactivated form of the pathogen that causes a disease to trigger protective immunity to it. There are two types of whole virus vaccines. Live attenuated vaccines use a weakened form of the virus, which can still grow and replicate, but does not cause illness. Inactivated vaccines contain viruses whose genetic material has been destroyed by heat, chemicals or radiation so they cannot infect cells and replicate, but can still trigger an immune response (Gavi W. , 2021).

However, live attenuated ones may risk causing disease in people with weak immune systems and often require careful cold storage, making their use more challenging in low-resource countries (Gavi W. , 2021).

B. Protein Subunit

Subunit vaccines or acellular vaccines is purified pieces of the bacterial pathogen that stimulate immune cells. In general, these specific pieces, called protein, produce a strong and effective immune response which minimize the risk of side effects. However, the subunit vaccines could make immune response weaker because the antigens used to elicit an immune response may lack molecular structures called pathogen-associated molecular patterns which are common to a class of pathogen. These structures can be read by immune cells and recognized as danger signals (Gavi P. , 2021).

C. Nucleic Acid

Nucleic acid vaccines use genetic material (DNA or RNA) from a disease-causing virus or bacterium to stimulate an immune response against it. This genetic material that contains specific nucleotides, linked in a long chain, inserted in the host cells in order to construct the antigens (protein), using protein-making machinery, and trigger an immune response (Gavi N. , 2021).

D. Viral Vector

Unlike other vaccines Viral vector-based vaccines does not have antigens, they use the spike proteins found on the surface of the virus as genetic instructions to produce antigens by delivering these genetic codes into the cell. Ones the cells received these instructions, large amounts of antigens will be produced using cellular machinery of the body and trigger an immune response. This has the advantage of triggering a strong cellular immune response by T cells as well the production of antibodies by B cells. However, since there is a chance that many people may have already been exposed to

the viruses being used as vectors, some may be immune to it, making the vaccine less effective (Gavi V. , 2021).

Meanwhile, National regulatory authorities authorized twenty-two COVID-19 vaccines. Six of those have been approved for emergency or full use by at least one WHO recognized stringent regulatory authority (Oxford–AstraZeneca, Pfizer-BioNTech, Sinopharm-BBIBP, Moderna, Sinovac, and Janssen)

1. Oxford–AstraZeneca

Oxford–AstraZeneca also called Vaxzevria and Covishield is a viral vector vaccine produced by the British University of Oxford, British-Swedish company AstraZeneca, and the Coalition for Epidemic Preparedness Innovations (Wikipedia, 2021).

Oxford–AstraZeneca is an mRNA vaccine that based on the spike proteins of the virus to construct the genetic instructions. After injecting these genetic instructions into cells, the immune system body will be triggered and produce antigens for the virus (Terry, 2021). AstraZeneca vaccine against Covid-19 is given by intramuscular injection in two doses (21 Days between the first and second dose) each dose of 0.5 ml contains: Chimpanzee adenovirus viral particles, GMOs, 2MG of ethanol per dose, 1Mmol of Sodium (Demmer, 2021). The efficacity of vaccine is about 95% and 100% at preventing hospitalization and death. Meanwhile, Lab data suggest “quite effective” against the UK variant as well as the South African and Latin American variants. Also, data suggests it is effective against hospitalization of the Delta variant but more data is needed (Terry, 2021).

2. Pfizer–BioNTech

The Pfizer–BioNTech COVID-19 vaccine, also known as Comirnaty or BNT162b2 is an mRNA vaccine produced by the German company BioNTech and the American company Pfizer. (Wikipedia, 2021) (David Bême, 2021). This vaccine requires 2 doses for maximum protection according to Health Canada at 21-day intervals (Vaccin de Pfizer-BioNTech contre la COVID-19 , 2021). Clinical trials have shown that from one week after the second dose, the Pfizer-BioNTech COVID vaccine was effective at approximately (Vaccin de Pfizer-BioNTech contre la COVID-19 , 2021) 95% to protect trial participants aged 16 and over from COVID-19, 100% to protect participants from 12 to 15 years old.

After a vaccine is given, it is common to have temporary side effects such as Pain, Redness and Swelling in the arm where you got the shot. Also, it might produce other effects like Tiredness, Headache, Muscle pain, Chills, Fever, Nausea. They usually last a few hours or days after vaccination because it is the body’s natural response that

goes together to build immunity against disease (National Center for Immunization and Respiratory Diseases (NCIRD), 2021).

3. Sinopharm-BBIBP

Sinopharm COVID-19 vaccine or BIBP vaccine, is one of two inactivated virus COVID-19 vaccines developed by Sinopharm's Beijing Institute of Biological Products (BBIBP or BIBP). Authorized in 31 December 2020 by China's National Medical Products Administration (Sinopharm, 2021). After injecting the inactivated virus in the body, it triggers the immune response that excites cells T And B to produce antibodies against this inactivated virus what earn the body immune against Covid-19 (Robert Carlson MD, 2021).

Like other vaccines The Sinopharm-BBIBP has some common side effects such as pain, fatigue, headache, lethargy, and tenderness (Robert Carlson MD, 2021). Clinical trials run by the state-owned company Sinopharm showed that it had an efficacy rate of 79% (Corum Jonathan, 2021).

4. Moderna

Like Pfizer-BioNTech vaccine, Moderna vaccine or Spikevax is a messenger RNA vaccine produced by the American company Moderna, the U.S. National Institute of Allergy and Infectious Diseases, the U.S. Biomedical Advanced Research and Development Authority, and the Coalition for Epidemic Preparedness Innovations. The vaccine authorized by the China National Medical Products Administration on December 31, 2020. This ultra-innovative technology consists of injecting strands of genetic instructions (messenger RNA) which will lead our cells to manufacture specific proteins or "antigens" for the coronavirus. These proteins will be identified by the immune system, which will then produce antibodies (Team, 2021). The vaccine requires 2-dose of β-propiolactone-inactivated at 21–28-day intervals. Each dose of 0.5 ml contains: 100 micrograms of messenger RNA (mRNA) encapsulated in the SM-102 lipid nanoparticles and other excipients (Moderna-NIAID, 2021).

AS the most common secondary effects of the vaccine were pain at the injection site, headache, and fatigue. However, other symptoms could be occurred such as nausea and inflammatory demyelination syndrome/acute disseminated encephalomyelitis (vaccines, 2021). The effectiveness of the vaccine against COVID-19 was 94.1% (Team, 2021).

5. Sinovac

CoronaVac, also known as the Sinovac COVID-19 vaccine, is an inactivated virus COVID-19 vaccine developed by the Chinese company Sinovac Biotech. It was Phase III clinical trailed in Brazil, Chile, Indonesia, the Philippines, and Turkey and

relies on traditional technology similar to BBIBP-CorV and Covaxin. In late August 2020, China approved CoronaVac for emergency use to vaccinate high-risk groups such as medical staff. In early February, China approved CoronaVac for general use(CoronaVac, 2021). The Sinovac CoronaVac vaccine does not need to be frozen, and both the vaccine and raw material for formulating vaccine doses could be transported and refrigerated at 2–8 °C (36–46 °F). CoronaVac is a 2-dose β-propiolactone-inactivated, aluminum hydroxide-adjuvanted COVID-19 vaccine administered on a 0/14-28-day schedule to prevent COVID-19 disease. A real-world study of millions of people who received CoronaVac found published by the WHO found the vaccine 67% effective against symptoms, reduced hospitalizations by 85%, intensive care visits by 89%, and deaths by 80% (Robert Carlson MD, CoronaVac COVID-19 Vaccine, 2021). CoronaVac has some side effects included fatigue, diarrhea, and muscle pain. Most of these side effects were mild and lasted only for 2 days (Jeong, 2021).

6. Janssen

The Janssen COVID-19 vaccine is a viral vector vaccine produced by Janssen Pharmaceutica (a subsidiary of Johnson & Johnson) and Beth Israel Deaconess Medical Center. It is also known as Johnson & Johnson COVID-19 Vaccine and as COVID-19 Vaccine Janssen (Wikipedia, 2021). The vaccine consists of a recombinant type 26 adenoviral vector (Ad26.COV2-S) incapable of replicating and expressing the Spike glycoprotein (also called S protein or spike protein) of the SARS-CoV-2 coronavirus (Janssen, 2021).

Unlike the other vaccines require two doses about 28 days apart, the Johnson & Johnson vaccine only requires a single dose. Since COVID-19 Vaccine Janssen has shown effectiveness of 66% in preventing moderate-to-severe COVID-19, 28 days after vaccination and 100% of efficacity ad preventing severe disease after day 49, it has been given conditional marketing authorization throughout the European Union on 11 March 2021, (Terry, 2021). The dose (0.5 mL) of Johnson & Johnson contains: Antigen with at least 8.92 log10 infectious units (I.U.) and genetically modified organisms (GMOs). Also, the product contains some excipients (Janssen, 2021). The most common side effects are pain at the injection site, headache, tiredness, muscle pain and nausea, they just occurred within 1 or 2 days after vaccination (EMA, 2021).

Conclusion

According to the latest development of the virus and the recent variants of this viral illness, several vaccinations were authorized by World Health Organization for emergency and general use. Due to the different categories of the vaccinations, various vaccinations are approved by different countries around world. As a result, the transmission rates and the numbers of new cases have reduced in many countries based on the percentage

of the vaccination. However, the comparison of the effectiveness of these vaccines is not clear because their clinical and preclinical studies were on different population. Moreover, it would be premature to hail the safety and immunogenicity observed in COVID-19 vaccine trials as a real success pandemic vaccine development paradigm (Mangalakumari Jeyanathan, 2020). Also, some variants are having a slight impact on the ability of vaccines to guard against mild disease and infection. Furthermore, vaccines can stop most people from getting sick with COVID-19, but not everyone. Even after someone takes all of the recommended doses and waits a few weeks for immunity to build up, there is still a chance that they can get infected. Vaccines do not provide full (100%) protection, so 'breakthrough infections' – where people get the virus, despite having been fully vaccinated – will occur (WHO, 2021).

Besides the importance of imposing public health and infection control measures to prevent or decrease the transmission of SARS-CoV-2, the most crucial step to contain this global pandemic is by vaccination to prevent SARS-CoV-2 infection in communities across the world. After being vaccinated, individuals should continue taking simple precautions, such as physical distancing, wearing a mask, keeping rooms well ventilated, avoiding crowds, handwashing for a minimum of 20 seconds with soap and water when they come in contact with contaminated surfaces, and coughing into a bent elbow or tissue, call for the emergency service in case of getting infected or sense that you have some symptoms of the virus.

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