EDITORIAL

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COVID-19 Variants and Vaccine Benefits-Risks Balance

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Since the emergence of coronavirus disease 2019 (COVID-19), the SARS-CoV-2 virus (the causative agent of the disease) has spread and imposed an enormous health burden worldwide. As of 27 July 2021, almost 200 million people were infected with more than 4 million deaths globally (according to WHO Coronavirus Dashboard, https://covid19.who.int/table). Although many treatment modalities have been used or still under trials all over the world, no specific treatment was found to cure or prevent the disease development. Therefore, immunization was regarded the best choice to prevent the development of the disease or at least reduce morbidity and mortality. Using the concept of herd immunity; that; with a threshold at 60 to 70% of the all population gaining immunity through previous exposure to the virus or by vaccinations; can control a very contagious disease. Owing to COVID-19 serious complications and millions of deaths worldwide with a great impact on the health care system, natural infection is an unsuitable option to reach population protection [1].

COVID-19 VARIANTS AND VACCINE EFFECTIVENESS

Currently, there are 8 approved COVID-19 vaccines in addition to approximately 98 at various stages of clinical development [2]. According to the Our World in Data, as of 28 July 2021, 28% of the world population has received a minimum of 1 dose of a COVID-19 vaccine with about 14.4% of the population are fully vaccinated. In low-income countries, only 1.1% of the population have received one dose (https://ourworldindata.org/covid-vaccinations).

The vaccine recipients showing a potent immune response after full vaccination which is measured by vaccine effectiveness (VE) [representing rates of disease among vaccinated individuals in comparison to rates in unvaccinated ones]. Although the types of vaccines have a certain degree of variance in the effectiveness, wide vaccination programs have proven to be highly effective as preventing symptomatic disease and reducing death rates. The VE for mRNA was found as high as 86.9% (95% confidence interval [CI]: 80.4-91.2%) with a breakdown as 84.3% (95% CI: 74.6- 90.3%) with Pfizer-BioNTech (Pfizer, BNT162b2) and 90.0% (95% CI: 82.0-94.4%) with Moderna (mRNA-1273). The viral vector vaccines showed 82% (95% CI: 63%-92%) with OxfordAstraZeneca (AZ or ChAdOx1 nCoV-19) and 66.3% (95% CI: 59.971.8%) with Johnson & Johnson's Janssen (J & J, J & J/Janssen, JNJ-78436735) [3, 4]. The interim results of phase 3 trial of SARS-CoV-2 inactivated vaccine in Turkey (CoronaVac) showed VE of 835% (95% CI: 654921%), while in the Gulf countries using WIV04 and HB02 vaccines showed 72.8% (95% CI: 58.1-82.4%) to 78.1% (95% CI: 64.8-86.3%) [5, 6].

In the fall of 2020, in addition to the ancestral strain, the US Centers for Disease Control and Prevention (CDC) released a data, published July 27, 2021, showed that the new emerged variants causing a new threat for the vaccination programs. The 2 groups of variants so-called variants of concern (VOC) and variants of interest (VOIs). Among VOC, the Delta variant (B.1.617.2), which has emerged in India is regarded the most virulent variant. The other notable variants include; Alpha (B.1.1.7), Beta (B.1.351), and Gama (P.1) which were first noticed in the United Kingdom (UK), South Africa, and Brazil respectively. The VOC have been spreading globally, constituting about 35-40% of infections in the US and the UK. The VOIs still lack clear proof of increased transmission, severity of the disease, or impact on available vaccines. This group of variants, VOIs, were firstly noticed in California-US (Epsilon; B.1.427/B.1.429), the New York-US

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(Iota; B.1.526), the UK and Nigeria (Eta; B.1.525), and in India (Kappa; B.1.617.1 and B.1.617.3) [4].

The CDC data showed growing evidence indicates that fully vaccinated individuals are at reduced risks, even caused by Delta variant, of severe illness, hospitalization and death from COVID-19 compared with unvaccinated people. However, VE was lower in preventing infection or symptomatic infection that caused by other variants in comparison with Alpha variant or the ancestral strain [4]. The VE of Pfizer or AZ vaccine was notably lower among people with Delta variant than those with Alpha variant (30.7%; 95% CI, 25.2-35.7 vs. 48.7%; 95% CI, 45.5-51.7); with similar results for both vaccines. Besides, the effectiveness was more after 2 doses than after one dose for both vaccines. With 2 doses of Pfizer, the effectiveness was 88.0% (95% CI, 85.3 to 90.1) among persons with the Delta variant and 93.7% (95% CI, 91.6 to 95.3) among those with the alpha variant. The effectiveness of 2 doses for AZ was 67.0% (95% CI, 61.3 to 71.8) and 74.5% (95% CI, 68.4-79.4) among persons with the Delta and Alpha variants respectively [7].

Data from the Public Health England (PHE), published a pre-print study [8], that estimated the risk of hospitalisation in a form of VE against hospitalization (VE = 1- OR of symptomatic disease x HR of hospitalization). The study demonstrated that the VE against hospitalization from severe COVID-19 after two doses of vaccine (Pfizer or AZ) was higher than one dose. In addition to that, VE of 2 doses was slightly lower among persons with the Delta variant than those with Alpha variant. VE with 2 doses, for Pfizer vaccine was 96% (95% CI, 86-99%) among persons with the Delta variant and 95% (78-99%) among those with Alpha and for AZ was 92% (95%, CI 75-97) and 86% (95% CI, 53-96) among those with Delta and Alpha variants respectively. Moreover, the effectiveness with 1 dose of Pfizer was 94% (95% CI, 46-99) among persons with Delta variant and 83% (95% CI, 62-93) with Alpha variants and for AZ, was 71% (95% CI, 51-97) and 76% (95% CI, 61-85) among those with Delta and Alpha variants respectively.

An unwelcome twist in the pandemic that some fully vaccinated people can carry big loads of the Delta variant with so-called breakthrough infections and can spread the virus to others just as readily as unvaccinated people. This finding played a role in renovated recommendations that every person, vaccinated or not, needs to wear masks indoors in certain public situations [9].

It was proposed that the vaccine has to have not less than 70% efficacy to prevent an epidemic and $\geq$ 80% to a larger epidemic without other measures; such as social distancing [10]. Hence, the vaccination is effective against severe infection, hospitalization and death caused by the VOC and no clear data for the disease caused by the VOIs which is still a matter of increasing importance.

VACCINES SIDE EFFECTS AND SAFETY

The COVID-19 vaccines are safe and effective and, as with other vaccines and medicines, are not free of side effects. The adverse reactions usually of mild to moderate and short-lasting which differ according to the specific vaccine. Most common effects include; fever, chills, headache, fatigue, muscle pain, pain at the injection site, and diarrhea [11]. Anaphylaxis was regarded as a rare safety warning (2-5 per million vaccinated) reported from the clinical trials, needs to be evaluated in patients with allergy to vaccines components and to be considered for all vaccinated people at the time of 1st dose. Myocarditis and pericarditis, a rare serious adverse events were reported after mRNA vaccines among people ages 30 and younger with a total number of 1,249, as of July 30,2021. A very rare events of Guillain-Barr Syndrome (GBS) were reported in around 143 after more than 13 million J & J vaccine doses administered [12].

In February 2021, a new safety signal of blood clot condition emerged with the AZ vaccine. A phenomenon resembles heparin-induced thrombocytopenia (HIT), which is so-called vaccine-induced immune thrombotic thrombocytopenia (VITT), thrombotic thrombocytopenic syndrome (TTS), or vaccine-induced prothrombotic immune thrombocytopenia (VIPIT). The features of the syndrome characterized by thrombosis (venous or arterial), mostly at unusual sites (cerebral and/or splanchnic veins) with consumptive coagulopathy laboratory features that include; thrombocytopenia, hypofibrinogenemia and elevated D-dimer. The subjects showed an association with positive anti-PF4 (anti-platelet factor 4). Later, mid of April 2021, similar conditions were reported in recipients of another adenoviral vector, J & J vaccine [13, 14]. VITT estimated incidence was 7 to 10 cases/million people with the AZ vaccine in the UK and about 3.2 cases with the J & J vaccine in the US [14].

Blood clot was regarded as a serious event associating the mRNA COVID-19 vaccines. A data, large preprint study from the UK, [15] estimated the incidence of cerebrovascular and splanchnic (Portal) veins thrombosis (CVT and PVT) among mRNA COVID-19 vaccines recipients. The study reported that the CVT incidence after receiving the mRNA (Pfizer or Moderna) vaccine was 4.1 per million people and 44.9 for PVT. The absence of key hematological laboratory data including anti-PF4 antibodies from the enrolled subjects limits the ability to confirm whether the mechanism is likely to be of VITT or not. Furthermore, the data showed that the incidence of CVT and PVT were significantly greater, more than 9.5 times, in confirmed COVID-19 than that observed with mRNA vaccines. With COVID-19 cases the CVT and PVT were 39.0/million people (95% CI, 25.2 to 60.2) and 436.4 per million people (382.9-497.4) respectively. With people who received mRNA vaccines the CVT was 4.1 cases/million people (95% CI, 1.1 to 14.9) and the PVT was 44.9 cases/million people (95% CI, 29.7 to 68.0).

In summary, currently, vaccination is considered as the best strategy to protect people from COVID-19 and prevent severe illness and death. There are few proved vaccine mild side effects and the possibility of very rare serious events of coagulopathy. However, vaccines have proved efficacious and safe and hopefully, be able to eradicate the devastating COVID-19 pandemic. Nevertheless, rapidly progressing updates of the era of COVID-19 pandemic are being continuously monitored.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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