



## Commentary

## Increasing reinfections and decreasing effectiveness of COVID-19 vaccines urge the need for vaccine customization

## ARTICLE INFO

## Keywords

SARS-CoV-2  
 COVID-19 vaccines  
 Epidemiology  
 Disease outbreaks  
 Public health

### 1. Background

The Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2) epidemic began in late December 2019 in the Hubei province of Wuhan, China, and the WHO labeled it a pandemic scenario in 2020 [1], eventually naming the disease caused by this virus COVID-19 [2]. According to WHO, more than 611 million individuals have been infected with this virus, and 6.5 million have died as a result of this illness [3], with the count continuing. Moreover, the ongoing COVID-19 pandemic and associated responses have tremendously impacted the health and economy across the world [4]. Therefore, researchers recommended the evidence-based management of COVID-19 from the very early phase of the pandemic [5]. The 73rd World Health Assembly approved a resolution in May 2020 acknowledging the significance of widespread vaccination as a worldwide public-health aim for preventing and ending SARS-CoV-2 transmission [6]. Numerous vaccinations have previously been created and used for preventative reasons, and several more are in the works, however, the effectiveness and adverse effects are currently being studied. Scientists have developed several COVID-19 vaccines for preventive measures, and many more are in preclinical development and clinical phases [7]. According to recent statistics, 23% of vaccines in clinical research require a single dosage, whereas 57% require two to three doses to achieve an effective antibody level and function against the virus [7]. As of September 21, 2022, at least three out of every four persons (>72%) in high-income countries and one out of every four people (>23%) in low-income countries had received at least one dosage of the approved vaccinations [8].

### 2. Reinfection and effectiveness of existing COVID-19 vaccines

Although immunization is regarded to be the best line of action among all essential interventions to prevent or combat COVID-19. According to WHO data, 11 vaccines are currently in clinical development [7]. There are several debates over the efficacy of various vaccine types on various variations in various places. Dr. Eli and colleagues revealed that during the outbreak of the delta variation of the SARS-CoV-2, vaccines such as the BNT162b2, mRNA-1273, and Ad26.COV2.S were

observed to have lower efficiency among vaccinated people [9]. Besides, these vaccines were found to be effective against SARS-CoV-2 infection in phase III trials, with 70.4% effectiveness of the ChAdOx1 nCoV-19 vaccine (AZD1222; Oxford-AstraZeneca) [10], 95% effectiveness of the BNT162b2 mRNA vaccine (Pfizer-BioNTech) [11], 94.1% effectiveness of the mRNA-1273 vaccine (Moderna) [12], and 50.7% effectiveness of an inactivated vaccine (CoronaVac) [13]. Thirteen-month Swedish research found that the vaccinations (BNT162b2, mRNA-1273, and AZD1222) had prolonged effects after the second dosage. However, following the omicron outbreak, the vaccine's potency began to wane [14]. Furthermore, a group of Canadian researchers observed that after the fourth dosage, the vaccination was more effective against the omicron type of SARS-CoV-2 than the third dose of an mRNA vaccine [15]. It has been shown that even after manufacturing antibodies, healed individuals may remain viral carriers for a length of time [16]. As a result, the two most serious issues of COVID-19 infection are reactivation and reinfection. Several studies have found that treated individuals are nevertheless at risk of reinfection or reactivation of the SARS-CoV-2 virus [17–23]. However, several investigations determined that reinfection occurs even after vaccination, even if the odds are extremely low [24] or because of an emergence of a new variation [9], suggesting that the danger is not eliminated. During the omicron outbreak in Iceland, intriguing research found that two or more doses of vaccination were linked with a slightly greater risk of reinfection compared to 1 dosage or fewer [25]. Furthermore, numerous investigations found that vaccination effectiveness against the delta (B.1.617.2) variation was lower than against the Wuhan (B.1) or alpha (B.1.1.7) variants [26]. Another research from a Massachusetts town found that 74% of 469 patients, predominantly infected with the delta strain, were completely vaccinated [27].

### 3. Challenges and opportunities in fighting COVID-19

The ugliest challenge among all the protective measures now against COVID-19 is the right protection against the very frequent mutations of the SARS-CoV-2 virus at the right time. The virus is being mutated very often within a very short time. To date, the variants of the virus found

<https://doi.org/10.1016/j.amsu.2022.104961>

Received 18 October 2022; Received in revised form 9 November 2022; Accepted 13 November 2022

Available online 17 November 2022

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are alpha (B.1.1.7), beta (B.1.351), delta (P.1), gamma (B.1.617.2), and omicron (B.1.1.529) which were between 2020 and 2021 [28]. The speed of mutation is too fast and mostly unpredictable. Therefore, the already-developed vaccines are the only way the prevention although they are not showing high effectiveness against all the virus strains. Reinfection reports are also found globally of which we mentioned some of the recent reports in the previous section. Rahman et al. reported that reinfection is normally developing because of the genetically different coronavirus variations [27]. Treatment strategies using antiviral drugs are another big challenge. Although some antiviral drugs show the effectiveness and lower the risk of disease severity and hospitalization, several side effects are reported frequently at the same time, and also it cannot be a demanded way to eradicate the infection. According to Matrajt et al., antiviral therapies can become a strategic weapon that, when combined with immunization, can considerably reduce COVID-19 hospitalizations and fatalities while also assisting in the management of SARS-CoV-2 transmission [29]. However, no concrete clinical trial data has been found regarding this treatment strategy. Despite the worst-case scenario, the pandemic taught us a lot about healthcare administration and emergency response tactics. Vaccine development typically begins with some fundamental preclinical research, followed by clinical trials with various phases, and finally a post-approval observational safety surveillance phase. The entire procedure might take up to ten years [30]. Because of the importance and rapid spread of COVID-19, clinical development of a new vaccine should be accelerated, but ideally without skipping any of the critical processes of preclinical research and human clinical development [31]. However, clinical trials in different areas, on different races, and different age groups might not be conducted properly following all the complex steps of developing vaccines probably due to tackling the pandemic situation worldwide. Besides, we could gather some knowledge to protect ourselves from various infectious diseases. Nevertheless, awareness of disease protection has increased. People could gather knowledge about vaccines and antiviral treatments for COVID-19 as well as other viral diseases. Despite all of the problems and lessons learned, we are still unable to demand that the vaccines produced to combat COVID-19 be fully successful in eradicating the virus.

#### 4. Urgent need for COVID-19 vaccine customization

Vaccines are often regarded as the most effective prophylactic measure against any infectious illness [32]. A vaccination that is 100% effective, provides lifetime protection, has no lethal side effects, is reasonably priced, and is widely available can be regarded as an ideal and desirable vaccine candidate [32]. However, no such high-quality vaccination has yet been developed to combat COVID-19. We can see that different vaccinations have varied side effects on people of different ethnicities and ages. Furthermore, none of the immunizations have long-term consequences; several doses are suggested for practically all vaccine categories. Again, no vaccination is effective against all forms of the virus. The availability of all types of vaccinations in all places is still inadequate. Until now, there have been several debates over the quality and usefulness of vaccinations. Furthermore, extensive research is still being conducted to investigate the effects of vaccinations and to decrease the negative consequences of vaccines. Not only are the effects or side effects of vaccinations a huge worry these days, but reinfection in vaccinated persons is also a serious problem. People become infected again after receiving immunizations, and the illness can become severe in particular patient groups. The likely causes of this worrying issue include the patient's immunity and/or physiological state, as well as the virus's frequent emergence of genetic mutations. Because vaccines are not entirely capable of providing extraordinary protection against viruses, vaccine customization and the development of technology or ideas to detect probable mutations in the viral genome and create vaccinations appropriately is a pressing requirement. Vaccine customization can be accomplished by optimizing the non-coding sequence for mRNA vaccines, adding adjuvant, and using standard nucleotide

sequence technology to optimize nucleic acid-based vaccines for increased effectiveness, increased T-cell-based immunity for longer protection against the SARS-CoV-2 virus, and minimizing or eliminating vaccine adverse reactions. The helpless people of the whole world as well as the health care sector are pointing to the eyes of the health science researchers to take the striking challenge to discover or optimize health-friendly, economic burden-free preventive measures such as vaccines and provide a beautiful risk-free healthy life.

#### 5. Conclusion

To summarize, vaccine customization is now a critical requirement for saving humanity from the lethal SARS-CoV-2 virus. Furthermore, given the current scenario, adequate evaluation of the synergistic effects of vaccination and antiviral medicine may be a timely issue. Besides, the world should learn from this circumstance how to manage or create preventative measures to combat such a lethal infectious illness load. The newly personalized or optimized vaccinations must be made available to the entire world as soon as possible. Otherwise, the re-developed vaccinations will be unable to defend the planet from its terrible claw owing to the spreading nature of the infection.

#### Ethical approval

Not applicable.

#### Sources of funding

No funding was required for the study.

#### Author contribution

Syed Masudur Rahman Dewan: Conceived the idea, performed data collection, and writing the initial draft of manuscript. Md. Rabiul Islam: Conceived the idea, revised and edited the manuscript, and supervised the whole work.

#### Registration of research studies

1. Name of the registry: Not applicable
2. Unique Identifying number or registration ID: Not applicable
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): Not applicable

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#### Consent

Not required.

#### Provenance and peer review

Not commissioned, externally peer reviewed.

#### Conflicts of interest

No conflict of interest declared.

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