Original Article

Investigating the Return Possibility of Covid-19 Mutated Strains and Role of Vaccination in Present and Future

Kambiz Sadegi[1,2], Dadkhoda Soofi[3], Hosein Mirshekarpour[4], Hosien Pormasoumi[5*]

[1]Department of Anesthesiology, Zabol University of Medical Sciences, Zabol, Iran.

[2]Pain Research Center, Department of Anesthesiology and Pain Medicine, Iran University of Medical Sciences, Tehran, Iran.

[3]Department of Medicine, Zabol University of Medical Sciences, Zabol, Iran.

[4]Department of Radiology, School of Medicine, Afzalipour Hospital, Kerman University of Medical Sciences Kerman, Iran.

[5*]Department of Infectious Diseases, School of Medicine, Zabol University of Medical Sciences, Zabol, Iran. E-mail: drhpm@yahoo.com

Abstract

Covid-19 has killed more than 7 million people in the world so far. With general vaccination in 2021, the severity of deaths decreased significantly, but after 6 months, new types of Covid-19 emerged and deaths incidence increased. Epidemiological studies showed that despite high number of deaths, vaccination has reduced the severity of the disease in population. Many researchers did not suggest injecting third and fourth doses due to antigenic changes of virus, but some countries, such as Iran, have continued vaccination. In America and European countries, it has been suggested that vaccination should continue only for high-risk people. Biological science has not rejected dangerous mutations for this virus and has prepared itself to face mutated species of this virus again. Certainly, vaccination is the most important way to deal with the virus in future; but despite millions of mutations in Covid-19 virus structure, the compatibility of vaccine with new viral antigens is important in order to provide effective vaccines with high efficiency.

Keywords: Mutation, Vaccination, Mutant, Coronavirus, Covid-19.

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INTRODUCTION

One of the concerns that can affect health system in future is discussion of Covid-19 mutation with a new shape and structure (1, 2). According to the studies conducted in the last two years, what is certain and what the world has faced is that this virus does not remain static and continues its struggle to survive and adapt to the environment (2). The same problem has caused an increase in the risk of death due to the emergence of new types. Covid-19 has killed more than 7 million people in the world so far. With general vaccination in 2021, the severity of deaths decreased significantly, but after 6 months, new types of covid-19 appeared and complications of death increased (2, 3). Molecular studies have proven that viruses are intelligent. When a new vaccine or drug is used, this virus mutates, because it wants to fight the effect of this drug and keep itself alive. Vaccination becomes resistant. Viruses can respond to invasion and environmental changes by changing their genetic structure. When patient's immune system is activated, it reacts against virus, and virus adapts and equips itself to resist (4, 5).

Viruses undergo millions of mutations in a short period of time with each mutation, and the effective mutations cause the virus to take a new form. It can be called English, South African, Indian and Brazilian virus (4, 6). Every day it enters a structure and with a new clinical symptom. The fourth wave of corona virus was English type, which caused many deaths, and after that, delta type entered Iran from border of Iraq. With the mutation of English and Delta types, whole world faced a new crisis and great damage was done. With the creation of a new wave of virus, people's lives and health are at risk, many people lose their lives, this is a great damage. After that, the closure of businesses and quarantine imposes great financial and emotional losses on people. The closure of educational centers and administrative centers will definitely have negative financial, psychological, social and cultural effects on the world (5, 7, 8).

Epidemiological investigations showed that despite the number of deaths, vaccination has reduced severity of disease in population. Many researchers did not suggest injecting third and fourth doses due to antigenic changes of virus. But some countries, such as Iran, have continued vaccination. Of course, paying attention to health principles according to instructions for prevention is an important issue. Vaccination based on new mutation antigens can be effective against viruses and other waves of infection (9, 10). Due to the importance of this issue, present study investigated the possibility of mutated covid-19 strains return and the role of vaccination in present and future.

Covid-19 Mutations

According to the structure and characteristics of Covid-19, occurrence of all kinds of mutations and different strains creation can be expected. So far, Covid-19 has had many mutations and created new variants. Indicator variants are classified into different groups based on the potential to cause disease, severity of disease, morbidity and/or mortality, rate of infection and response to covid19 antibodies as well as vaccination (11). This category includes: VOI, VOC and VOHC, which are divided into other subgroups (Table 1).

Table 1: Classification of covid-19 variants (2)

Pango lineage and WHO nomenclature	Specification
_ B.1.525 (Eta) _ B.1.526 (Iota) _ B.1.617.1 Variants of Interest _B.1.617.3(Kappa) _ C.37 (Lambda) ˆ _ B.1.621 (Mu)	• Changes in receptor binding • Reduced neutralization by antibodies produced from previous infection or vaccination • Reduced treatments effectiveness, potential diagnostic impact, predicted increase in transmission and disease severity • Outbreak or limited spread in United States or other countries
_ B.1.1.7 (Alpha) Variants of concern _ B.1.351 (Beta) _ P.1 (Gamma) _ B.1.617.2 (Delta)	• Increasing the ability to transmit disease • Significant reduction in neutralization by antibodies produced during previous infection or vaccination • Reducing the effectiveness of treatments or vaccines • Widespread interference with diagnostic testing purposes, reducing vaccine-induced protection against severe disease
Variants of high consequences _ None (as of 17th September 2021)	• Failure to diagnose • Significantly reduced vaccine efficacy, high number of vaccine breakthroughs, and very little vaccine-induced protection against disease • Significant reduction in response to approved treatments and severity of clinical disease Increased hospitalization

According to reports as of September 2021, alpha, beta, and delta strains appear to be among the most common Covid-19 mutant variants worldwide. However, strain B.1.1.7 has been reported as the most common variant in United States (12). The signs and symptoms of the variants obtained from Covid-19 can be seen in Table 2 (13).

Table 2: Signs and symptoms of variants obtained from Covid-19

Signs and symptoms	Main variant (%)	(%) VOI	(%) VOC	VOHC (%)
cough	28		35	
fatigue/weakness	29		32	
Headache	30		32	
Muscle pains	21		25	
Sore throat	19		22	
Fever	20		22	
Loss of taste	19		16	
Loss of sense of smell	19		15	
Ability to transmit disease	Yes	No	Yes	Yes
Illness severity	fewer	fewer	More	More
Failure of diagnostic tests	No	No	No	Yes
treatment		Potential reduction in neutralization by monoclonal antibody therapies	B.1.1.7 variants have lowest response to treatment, while P.1, B.1.351 and B.1.427, B.1.429 variants have a significant effect on EUA treatments and monoclonal antibody treatments, respectively	
Vaccine effectiveness	Pfizer, Moderna, and Janssen are effective	Potential reduction in neutralization by serum after vaccination	Minimal effect on post-vaccination neutralization for strain B.1.1.7, while other variants have moderate reductions in post-vaccination neutralization.	They have a significant effect on neutralization after vaccination.
Notification to WHO and CDC	No	No	Yes	Yes

In general, all mutations created on covid-19 virus are in its antigen section, and amino acid changes affect antibody neutralization. In fact, amino acid substitutions and deletions exist at a high and significant level in global virus population and affect antiviral antibodies; Meanwhile, there is new evidence that mutant variants are resistant to vaccination immunity, which indicates a decrease in vaccines effectiveness over time. Therefore, a comprehensive consequence understanding of mutation spike (antigenic) and T cell-mediated immunity and non-spike epitopes recognized by antibodies is important. In general, a broader understanding of mutations phenotypic effects in covid-19 genome and their consequences will help to clarify the factors of transmission and evolutionary success for development of better vaccines (14, 15).

One of the important things that provides the basis for variants creation and leads to new species emergence silently in world and can cause public concern in whole world is the lack of suitable facilities for sequencing and checking different variants. In fact, the lack of appropriate sequencing techniques in some countries creates a limitation in implementation of further studies regarding identification of new variants nature due to financial and economic crisis in these countries, and this issue can become a crisis for the whole world (16).

Vaccination Reduces the Severity of the Disease

Epidemiological investigations showed that despite the number of deaths, vaccination has reduced the severity of disease in population. In fact, vaccinations prevent and protect against infection and disease, especially in vulnerable populations. In the context of the outbreak of new coronaviruses, vaccines help to control and reduce disease transmission by creating general immunity in addition to protecting healthy people from infection. However, there are economic, social, and clinical barriers to vaccination programs. Among these obstacles, we can mention the desire of the general public to be vaccinated with a new vaccine, side effects and severe reactions of vaccination, the potential difference or low efficiency of the vaccine in different populations compared to a clinical trial population, and the availability of the vaccine. Of course, despite all these obstacles, it should be said that vaccination has played a role in reducing the spread and is considered one of the important factors for managing the spread of Covid-19 (17).

To date, many vaccines have successfully passed laboratory stage and reached mass production. In this regard, America, Russia, Australia and Canada have provided vaccines with reasonable immunity. Vaccines under development include: Vaccines based on viral vector, DNA vaccine, subunit vaccine, vaccine based on virus-like particles (VLPs), vaccine based on whole virus (Inactivated Whole-Virus, inactive IWV) and live attenuated vaccine (11, 17). Meanwhile, some vaccines are made based on viral surface protein (18).

Covid-19 vaccine has changed the course of epidemic. In total, 162 doses were estimated for every 100 people worldwide. In countries that have reached the highest level of vaccination, death rate is significantly reduced. Meanwhile, at the end of 2021, omicron type became famous and surprised the world. Omicron was somewhat more intense than previous variants, but spread much faster. Millions of vaccinated people became ill from omicron strain, but vaccines served their most important function of preventing severe disease. During Omicron pandemic, booster vaccination reduced the chance of hospitalization and death by more than 90%. A sudden increase in cases of the rapid type has strained health systems, but the average outlook for Covid-19 patients has improved significantly (19).

Vaccination Status in the World

Since the emergence of covid-19, several vaccine methods have been reported and four main models have been used in making these vaccines (20). The first type is completely based on virus, which is designed in two forms: a weak live virus and an inactive virus. A number of eight vaccines, such as those of Iran (Barekat), India (Bharat) and China (Sinopharm), have been made on this basis. The second type is based on viral vector that 16 vaccines such as British (Astrazenca), Russian (Sputnik) and another vaccine from China are made according to this model. The third type is based on nucleic acid (DNA/RNA). Moderna and Pfizer vaccines are designed based on this model. The fourth type of inactivated vaccines that are based on viral protein, which can also be called the French vaccines, Iran-Cuba Pasteur Institute vaccine (Sanofi) and America's Novavox (20).

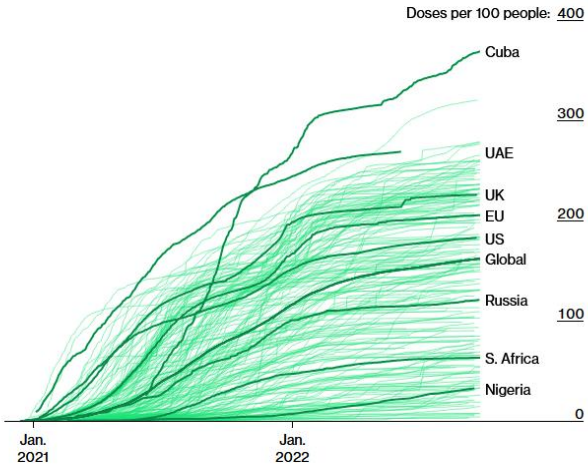
In early 2021, Israel showed for the first time that vaccines reduce covid-19 infections, and cases have declined rapidly. A similar pattern of vaccination and recovery was repeated in dozens of countries. New transmissible strains caused more outbreaks, but in these subsequent waves, unvaccinated patients faced a higher risk of hospitalization and death. This disparity in outcomes has led health officials to call the current stage of Covid-19 an "unvaccinated epidemic ". Since the start of global vaccination campaign, countries have experienced unequal access to vaccines and varying degrees of success in vaccinating the population (19).

Recent clinical research has shown that the frequency of confirmed COVID-19 and severe disease is significantly reduced with the third and fourth doses of inactivated or mRNA vaccine. Other research also supports the ability of booster vaccination to increase antibodies titers that significantly neutralize SARS-CoV-2 strains. As a result, infectious disease specialists have carefully examined whether booster shots are necessary for all susceptible individuals or only for a few vulnerable groups to increase immunity and protect against new mutations. Hence, it is expected that booster doses of Covid-19 will be met with rejection or skepticism, which requires thorough exploration

of the underlying causes of such attitudes (21–24).

In a survey conducted on 13 countries in Mediterranean region, it has been seen that only 26.7% had a positive opinion about vaccination, and as a result, they are less agreeable to booster vaccines. Of course, this confidence was higher in high-income countries compared to low- and middle-income countries (25). In America and European countries, it has been suggested that booster vaccination should continue only for high-risk people. Meanwhile, Cuba leads the world with 369 prescribed doses per 100 people (19).

Studies on acceptance of booster COVID-19 vaccine doses in EMR are scarce. A study in Jordan reported that about 50% of population were concerned about vaccination side effects that might prevent them from receiving booster shots, and 45.3% thought that receiving a third dose of vaccine would exacerbate side effects (26). Greater acceptance of booster vaccination has been reported among health care workers in Saudi Arabia; Thus, about 71.1% of 2059 health care workers accepted booster doses. This study showed that factors such as having co-existing conditions, higher education level, high income and being single are very effective in accepting a booster dose of the vaccine (27).



Note: Several countries, including Cuba, use vaccines that require three doses for the primary series. Data is from Bloomberg's Covid-19 Vaccine Tracker (19).

The Point of View of Biological Science about the Possibility of Mutation

Biological science has not rejected dangerous mutations for this virus and is ready to face the mutated species of this virus again. However, virus is changing at a much slower rate than HIV, possibly due to a "corrector" enzyme that corrects potentially fatal copying errors. According to Hudcroft, a molecular epidemiologist at the University of Basel, Switzerland, a typical SARS-CoV-2 virus accumulates only two single-letter mutations per month in its genome, a rate of change roughly half that of influenza and one-fourth that of HIV (28).

Despite the virus's slow rate of mutation, researchers have cataloged more than 12,000 mutations in SARS-CoV-2 genome. But scientists can detect mutations faster than they can understand them. Many mutations have no consequence on the virus's ability to spread or cause disease because they do not change the shape of the protein, while those mutations that do change the proteins do more harm than good to the virus (28).

Vaccination in Present and Future

Vaccines and treatments are essential tools to control and fight COVID-19 pandemic. Achieving and sustaining a strategy to control virus is seen with faster development and more efficient deployment of medical countermeasures. The increase in progressive infections has been attributed to reduced vaccine-induced immunity and introduction of SARS-CoV-2 subtypes, necessitating consideration of vaccination booster doses. Boosters have been shown to be safe and effective in increasing SARS-CoV-2-specific neutralizing antibody levels (29).

As mentioned, vaccination is still ongoing in some countries, but it is done for disabled people and volunteers. But in the future, vaccination is a very important issue. Especially with new mutations of the virus, there is a possibility of creating another wave of transmission of this virus, and certainly vaccination is the most important way to deal with the virus in the future. Health organizations and vaccine producing bodies must be prepared to provide a new vaccine that is compatible with the new mutated strains of the virus.

Currently, by mid-March 2022, 57.05% of the world's population has been fully vaccinated, and 65.3% of United States of America (USA) population is fully vaccinated; While 76.7% have received at least one dose of the vaccine. Although manufactured vaccines are up to 95.0% effective, their effectiveness declines over time, indicating the need for booster doses. Also, vaccination has not been able to prevent "precursor" infections. Due to the novelty of the virus, many questions regarding the long-term reactivity of these vaccines remain unresolved. The limitations of SARS-CoV-2 vaccines suggest that additional measures are needed to ensure definitive control of the COVID-19 pandemic. Therefore, the Food and Drug Administration (FDA) has issued emergency use authorization (EUA) for the use of certain therapeutic agents because they have demonstrated significant clinical results (30).

CONCLUSION

The Covid-19 virus continues to mutate. Biological science has not rejected dangerous mutations for this virus and is ready to face mutated species of this virus again. Researchers have cataloged more than 12,000 mutations in SARS-CoV-2 genome, which could trigger a new pandemic if a dangerous mutation occurs. The omicron mutation showed that there is a possibility of creating dangerous

variants. Some countries have ordered booster doses of vaccination for coming winter. However, there are many concerns related to vaccination side effects that the need to inform people about vaccination safety and its importance is felt. Vaccination is the most important way to deal with the virus in future, but despite millions of mutations in structure of Covid-19 virus, it is important to produce vaccines against new viral antigens in order to provide effective vaccines with high efficiency. Health organizations and vaccine producing bodies should be prepared to provide a new vaccine that is compatible with the new mutated strains of virus.

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