The Experience of COVID-19: Variants, Vaccines and Policies

Jiajuan Han*

University of Melbourne, Melbourne, Australia

*Corresponding author: 18403015@masu.edu.cn

Abstract. Since the new coronavirus epidemic broke out at the end of 2019, the virus has brought several problems, both in people's lives and countries' development. This article will recommend the overall situation from three aspects, SARS-CoV-2 and Variants, vaccines, and policies. Firstly, we should make efforts to reduce the chance of superspreading events occurring, therefore preventing the evolution of SARS-CoV-2. Then governments and big companies will need to be more ambitious in developing different kinds of vaccines. Finally, the best suit policies should enact to make limited resources maximum used. That information would give the reader some inspiration to cope with the epidemic, furthermore, they can also learn some lessons from other countries, and find a suitable way to control the spreading of the virus.

Keywords: SARS-CoV-19, Variant of Concern, vaccine, dynamic zero-COVID policy, zero-tolerance border quarantine.

1. Introduction

In the past two years, people's lifestyles have changed dramatically because of the COVID-19, and we have been unable to move or travel freely. Even more, over 494 million verified cases have been reported, and over 6 million people have lost their lives as a result of this virulent virus [1]. We are all looking forward to the conclusion of the pandemic and the restoration of normal life as soon as possible. Therefore. This article summarizes the current situation from SARS-CoV-2 and mutations, Vaccines, and policies in those three aspects, furthermore, some experiences which can help people get through this together.

To begin with, Coronaviruses are various groups of single-strained, positive-sense RNA viruses, the specific structure results in the high ability to mutant. Besides that, the super spreading of COVID-19 effects on facilitates the randomness effect of the genetic drift [2]. Those emerging mutant strains of SARS-CoV-2 variations, including B.1.1.7, B.1.617.2, B.1.351, P.1, B.1.1.529.1, etc., become smarter to evade the immune system and increase infective capabilities reflects on the ineffectiveness of current vaccines [3].

Afterward, Vaccination is identified as the crucial cornerstone of prevention and fighting SARS-CoV-2 infection, which plays a big role in both limiting viruses spreading and lightening the symptom. So, a number of companies have developed different kinds of Vaccines. In China, most of them are inactivated vaccines. Besides that, there are also different kinds of vaccines injected in other countries such as mRNA vaccines and DNA vaccines. But we cannot be overly optimistic about the current situation, because the perpetual crisis of SARS-CoV-2 variants brings new problems to current vaccines, therefore the vaccines should keep developing.

At last, the high-effect policies are key to controlling the spreading. In China, a dynamic zero-COVID policy, and zero-tolerance border quarantine systems are being actualized strictly, which can limit the happens of several superspreader events, furthermore, reduce the risk of variant appearance. As we know, the COVID-19 epidemic is a global public health issue. The governments and global organizations need to strengthen global cooperation to tide over the difficulties together.

2. Variants

2.1. SARS-CoV-2

SARS-CoV-2, a kind of single-stranded RNA enveloped virus, is classified in the Betacoronavirus-CoV class of human coronaviruses. The coronaviral genome is consist of four main structural proteins: the spike (S), membrane (M), envelope (E), and nucleocapsid (N) protein. More specifically, the spike protein determines virus entry into cells by mediating attachment with Angiotensin-converting enzyme 2 (ACE2), a kind of host cell surface receptor. Therefore, the S protein determines the infectivity of the virus and its transmissibility in the host [4]. This protein is the main antigen-inducing protective immune response, and all vaccines under development target it, as a result of its special character, that can induce the antigen-protective immune response [5].

Another key point to remember is that several genetic variants of concern (VOC) of the virus have emerged in the process of several super spreader events [6]. These variants are assumed to provide higher transmissibility to the virus in a given epidemiological environment and some could also lead to higher severity, as a matter of fact, The high rate of errors occurring in the SARS-CoV-2 because of the single-strain structure, which may cause amino acid changes, truncations, or loss of viral proteins with implications. Meanwhile, the mutation variants may get a fitness advantage that can be selected over time. Besides that, the interaction between variants and host cells' surfaces might be strengthened, and even impact known viral antagonists of host defenses. furthermore, some special mutations, which have the ability to evasion of adaptive immune responses, would be selected over time, further challenging vaccine development [7].

2.2. Variants of concern

Currently, four main VOCs are listed, B.1.1.7 (Alpha), B.1.351 (Beta), B.1.617.2 (Delta), P.1 (Gamma), and B.1.1.529.1 (Omicron) (Figure 1). More specifically, all of them have a common feature --the accumulation of specific mutations in surface spike protein, The spike protein of SARS-CoV-2 has been enduring mutation in process of spreading, including C-terminal S1 subunit (CTS1) and Spike 2 (S2) variant mutations, nucleotide triphosphate (NTD) variant mutations, and receptor-binding motif (RBD) variant changes. Under this condition, the combination of Spike protein with human angiotensin-converting enzyme 2 (ACE2) might be changed even greater.

	RBG variant changes							
	K417N/T	E484K/A	N501Y	D614G	L452R	P681R	T478K	other
B.1.1.7 (Alpha)								
B.1.351 (Beta)	K417N	E484K						
P.1 (Gamma)	K417T	E484K						
B.1.617.2 (Delta)								
B.1.1.529.1 (Omicron)	K417N	E484A						G339D, S371L, S373P N440K, G446S, S477N Q493R, G496S, S375F Q498R, Y505H

Figure 1 Reported RBD substitutions in each variant of concern. The color means this kind of variant has a specific variant change.

B.1.1.7 (Alpha) was identified with 22 mutations, 9 of which are S protein mutations. N501Y is one of them, shown to process increased infectivity because its RBD binds to the ACE2 receptor 1.98 times stronger compared to the orient strain. Moreover, the combined action of N501Y and D614G leads to increased airborne transmissibility [8].

B.1.251 (Beta) is defined by 18 mutations including 8 Spike (S) mutations, whose infectivity is the same as B.1.1.7 due to N501Y and D614G, however, B.1.351 demonstrates a significantly higher impediment to neutralization through the convalescent and post-vaccination sera. which may result in E484 and K417N [8].

P.1 (Gamma) has the same mutations (e484K, n501Y, and D614) compare with B.1.251. The differences are K417T and H655Y (in the Spike substitutions), which may be the main reason for

double virus infectivity, further their synergistic effect may enhance this effect. Besides that, K417T and H655Y can lessen the sensitivity to multiple mAbs [8].

B.1.617.2 (Delta) appeared with 24 mutations, 8 of 24 are Spike protein mutations. Notably, it lacks N501Y which makes it different from other VOCs. L452R mutations have a higher affinity to attach to the ACE2, which reduces the Sensitivity of vaccine-stimulated antibodies. This character may lead to the invalidation of existing vaccines. moreover, this may help the delta variant to evade the attack from CD8 T cells. P681R could help superior fusion and even integration between the virus and the host cell by activating the spike proteins S1, and S2 [9].

Omicron is really special from other VOCs and characterized by 60 variants and 15 of them are RGB mutations. 23 unique omicron mutations are never found in other variants before. Those new RGB mutations play a greater role in increased binding ability of RBD with ACE2, immune escape, transmission potential as well as pathogenicity. Notable, N protein mutations may contribute to improving the expression of subgenomic RNA and raising viral loads. There are three sublineages of Omicron including BA.1 (B.1.1.529.1) which is a standard sub-lineage, BA.2(B.1.1.529.2), and BA.3(B.1.1.529.3) are rare subvariants. The transmissibility of omicron is seven times that of alpha, and one-fifth of all global COVID-19 infections are BA.2 cases [10]. It could, in particular, avoid most of them hitching, rather than all of them, licensed monoclonal antibodies, furthermore interfering with the interaction between ACE2 and spike.

3. Vaccines

As proven by past infectious pandemics, the vaccine seems like the most effective tool in controlling virus spread, making the immune system capable of against the virus [11]. Furthermore, specific drugs are still in development due to the contagious variety of COVID-19, accelerating the process of vaccine development is crucial to controlling the outbreak [12]. In China, Clinical studies have begun for 13 vaccine candidates. And six of them are in phase III clinical trials at current. What's more, there are five development-approved paths of vaccines in the world including inactivated vaccines (most widely used in China), mRNA vaccines (most effective), DNA vaccines, non-replicating viral vector vaccines, as well as protein subunit vaccines. Three of them deserve our attention. There are three kinds of vaccines that would be illustrated including inactivated vaccines, mRNA vaccines, and DNA vaccines.

Inactivated vaccines are most abroad used in China, made from killed microorganisms as well as a mature development platform, which have obvious stability advantages and are easy to transfer and store. What's more, the efficiency of inactivated vaccine is 72.8–83.5% [13] just following the mRNA vaccine. However, it is less immunogenic, hence it must be inoculated with nigher amounts of vaccine or associated with an adjuvant. some clinical trials are run in China including Sinovac Biotech, Sinopharm, Wuhan Inst Biol Products, and Chinese Acad Med Sci [14].

MRNA vaccines have the ability to stimulate cells to produce antigen protein coded by mRNA which is S protein, its variants, or fragments. When mRNA comes into cells, it must be carried by liposomes or Nanoparticles. As a novel vaccine type, the mRNA vaccine was with the highest efficacy (94.5–95%) [13], furthermore is also safe and simple to produce, and for this reason, that is a suitable candidate for an emergency vaccine [14]. In spite of that, A South African study discovered that the BNT162b2 vaccine has a 70% protective efficacy against Omicron. which had an evidently decreased compared with Delta with 93%. Thereupon the medical institution needs to strive to refine the existent vaccines [15]. However, China has not developed this kind of vaccine yet, which can be tested in phase III clinical trials.

DNA vaccines take effect by transmitting the virus DNA from plasmids to human-cell, then cells can produce antigen proteins. This vaccine king provides a significant deal of flexibility in terms of manipulating the coded antigen, However, exists the risk of tumors, if the plasmid DNA were not to integrate as expected [14].

The vaccine has helped people resist attacks from the virus, nevertheless, the appearance of VOCs leads to vaccine efficacy (VE) decreasing rapidly. Despite that current COVID-19 vaccines are effective, financial support is still needed to be put into vaccine development.

Notable, the novel variants have developed in the human population through multiple selections, which may lead to vaccine-breakthrough injection, however, the huge effect still is taken by the vaccine. According to China CDC Weekly (2022), those who received the entire immunization or a booster dose had a significantly lower incidence of Delta-variant and omicron-variant COVID-19 pneumonia. In conclusion, Vaccination is still a cost-effective and efficient manner against the attraction of COVID-19 as well as the high protective effect of vaccines needs to be continually developed to resist the perpetual appearance of new variants.

4. Policies

The function of the government and global cooperation also cannot be ignored who are the main performers that achieve the aim of controlling the global COVID-19 epidemic. The data suggest that the SARS-CoV-2 super spreading contributes to the randomness effect of the genetic drift accordingly increasing the chance of new VOC appearance. Therefore, the policies should be polished to avoid super spreading happening and make vaccines be used rationally.

In China, the government mainly takes two strategies, a dynamic zero-COVID policy, and zero-tolerance border quarantine systems. Firstly, dynamic zero-COVID-19 is the general policy of epidemic prevention and control. Specifically, when a local case appears, plenty of integrated measures would be taken to guard against the virus spreading or infecting other people. For example, targeted epidemic control is a typical policy. The concrete measures include Precisely preventing the spread of objects and accurately delineating the scope of the epidemic area; Enhancing detection to accurately carry out epidemiological investigations, enhancing nucleic acid detection in the board coverage; Strengthening the monitoring of virus mutation. This strategy has been broadly approved by other countries and native people.

The second one is zero-tolerance border quarantine systems which means the border should take strict policy to strict border measures to limit the risk of disease transmission from international travelers. This has successfully controlled the outbreak which is reliant on targeted test-trace-isolate-quarantine (TTIQ) responses. In fact, the policy exists a drawback while achieving huge success in epidemic control, it brings enormous economic and social costs. Besides that, Due to quarantine capacity limits, several citizens have been stuck abroad. As a result, the quarantine system must concentrate on balancing the advantages of decreasing import risk in contact with the related expenses while designing. In the case of COVID-19, If some countries have a willingness to relax current strict measures in border controls in the future, the continuous development and deployment of effective vaccines are required [16].

However, in relation to SARS-CoV-2, the functions of border quarantine systems and low levels of community vaccination are separated, which means those two things are not complementary. So, the aim of universal vaccination still needed to realize. This aim should be considered a common view not only in China but also the other countries. A high rate of vaccination could reduce the happen of superspreading and decrease the chance of the appearance of mutations, such as Omicron has brought several challenges to global people. According to a statistic data shows that full-dose target population coverage in Africa is only 14.1% which is one-sixth of the Western Pacific (86.5%). Even as production capacity increases, a massive imbalance in demand raises worries about the inequitable access to vaccines [17]. even though the production capacity of vaccines is increasing, the vaccines of supply and demand imbalance still raise people’s concerns.

5. Conclusion

In conclusion, this article sums up several pieces of information from the epidemic breakout till now. the control of COVID-19 cannot leave without the development of vaccines and suitable policies. The VOCs bring negative influence and challenges to existing vaccines so control of spearing and avoiding the superspreader event should be put in the first line. From this aspect, The dynamic zero-COVID policy and zero-tolerance border quarantine systems in China have made some achievements and been approved broadly, which could give other countries ideas to fight the epidemic. On the other hand, governments and pharmaceutical companies need to put more funds into vaccine development to fight new variants. The combined action can highly restrict the possibility of variation. Specifically, vaccines reduce not only the prevalence but also disease severity. What's more, the policies make vaccines used reasonable. However, COVID-19 is a global public health issue. To beat down the epidemic global cooperation also is necessary. As a consequence, people should consider those three aspects and find the best way to control the epidemic and get life back on track.

References

[1] Coronavirus [EB/OL]. World Health Organization [2022-04-16]. https://www.who.int/health-topics/coronavirus#tab=tab_1Fangfang.

[2] Forchette L, Sebastian W, Liu T. A Comprehensive Review of COVID-19 Virology,Vaccines, Variants, and Therapeutics [J]. Curr Med Sci, 2021, 41(6): 1037-1051.

[3] Gómez-Carballa A, Pardo-Seco J, Bello X, et al. Superspreading in the emergence of COVID-19 variants[J]. Trends Genet, 2021, 37(12): 1069-1080

[4] Li Q, Wu J, Nie J, et al. The Impact of Mutations in SARS-CoV-2 Spike on Viral Infectivity and Antigenicity [J]. Cell, 2020, 182(5): 1284-1294

[5] He Y, Zhou Y, Wu H, et al. Identification of immunodominant sites on the spike protein of severe acute respiratory syndrome (SARS) coronavirus: implication for developing SARS diagnostics and vaccines [J]. J Immunol, 2004, 173(6): 4050-4057

[6] Zhao S, Shen M, Musa S S, et al. Inferencing superspreading potential using zero-truncated negative binomial model: exemplification with COVID-19 [J]. BMC Med Res Methodol, 2021, 21(1): 30.

[7] Plante J A, Mitchell B M, Plante K S, et al. The variant gambit: COVID-19's next move [J]. Cell Host Microbe, 2021, 29(4): 508-515

[8] Park G, Hwang BH. SARS-CoV-2 Variants: Mutations and Effective Changes[J]. Biotechnol Bioprocess Eng, 2021, 26(6): 859-870.

[9] Shiehzadegan S, Alaghemand N, Fox M, Venketaraman V. Analysis of the Delta Variant B.1.617.2 COVID-19 [J]. Clin Pract, 2021, 11(4): 778-784.

[10] Chekol Abebe E, Tiruneh G, Medhin M, et al. Mutational Pattern, Impacts and Potential Preventive Strategies of Omicron SARS-CoV-2 Variant Infection [J]. Infect Drug Resist, 2022, 15: 1871-1887.

[11] Trovato M, Sartorius R, D'Apice L, et al. Viral Emerging Diseases: Challenges in Developing Vaccination Strategies [J]. Front Immunol, 2020, 11: 2130.

[12] Chen L, Cai X, Zhao T, et al. Safety of Global SARS-CoV-2 Vaccines, a Meta-Analysis [J]. Vaccines (Basel), 2022, 10(4): 596.

[13] Hadj Hassine I. Covid-19 vaccines and variants of concern: A review [J]. Rev Med Virol, 2021, e2313.

[14] Forni G, Mantovani A. COVID-19 Commission of Accademia Nazionale dei Lincei, Rome. COVID-19 vaccines: where we stand and challenges ahead [J]. Cell Death Differ. 2021, 28(2): 626-639.

[15] Collie S, Champion J, Moultrie H, et al. Effectiveness of BNT162b2 Vaccine against Omicron Variant in South Africa [J]. N Engl J Med, 2022, 386(5): 494-496.

[16] Zachreson C, Shearer F M, Price D J, et al. COVID-19 in low-tolerance border quarantine systems: Impact of the Delta variant of SARS-CoV-2 [J]. Sci Adv, 2022, 8(14): eabm3624.

[17] Viana R, Moyo S, Amoako D G, et al. Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa [J]. Nature, 2022, 603: 679-686.