International Journal of Microbial Science, ISSN (online):2582-967X, Volume 1, Issue 1, April 2020, pp.1-6
Available online at https://internationaljournalofmicrobialscience.com/

Review

Can Coronaviridae Viruses Reappear with their Novel Variants in Upcoming Years?

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Article Info

Article history:
Received: March 31, 2020
Accepted: April 13, 2020
Published: April 22, 2020

Keywords: SARS-CoV2, COVID-19, Mutation, genetic makeup, SARS-CoV.

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Abstract

SARS-CoV2, the infectious biological entity has made havoc across the globe and created a question mark on the survival of humans. This infectious agent is a variant of SARS-CoV spread in 2003 and more dangerous than previous infectious particles belonging to the same family. Biological objects get a mutation in their genetic makeup which is either beneficial or harmful. If a mutation is useful, the entity is selected by nature for survival. Such genetic changes are continuous processes, and organisms generate their variants. In this review, we have highlighted whether this theory is true regarding SARS-CoV2 or not. We have estimated the probability of reappearance of coronaviridae members in future with their variant forms.

1. Introduction:

In human history, there are many cases of viral pandemic infections including polio [1], ebola [2], smallpox [3], chicken pox [4], HIV-AIDS [5], which had put human life on serious risk [3]. Nevertheless, owing to efforts taken by medical sectors across the globe, such diseases were controlled by either vaccine [6] or treatments [7] or some of them are reduced by prevention only [8].

The diseases mentioned above were life threatening and caused a potential biological loss in the world [9,10,11]. Of them, airborne and contagious diseases [12] are more challenging to humankind since they are challenging to control. It is true, especially in those countries where the population is high, and awareness among people is less. Like other biological species, viruses are capable of altering their genetic makeup [13,14] and get chances of reappearances [13,14,15], hence making them more infectious than their parents [16]. The variation in genes results in altered protein sequence leading to changed functions of proteins [17]. The antiviral drugs available against these infections are not as productive as those were made to recognize only specific target sites [18]. As a result, the infectious particles go on infecting people continuously resulting in international health concern and panic with uncontrolled deaths.

According to Prajapat, M. et al. [19], there is only one Protein Data Bank (PDB ID:6LU7) on the 2019-nCoV, which forms a complex with the N3 inhibitor. However, the genome sequence shows that there is 95% similarity with the bat -SL-CoVZC45 and 88% to

SIRS CoV-ZSc [19]. This study suggests that the changes have occurred in the amount of recombination process in 2019-nCoV and the protein structural and functional levels.

In this review, we analyzed the evolution of corona virus family (Coronaviridae) [20] to know the genetic similarity and variation patterns in relation with newly arrived Severe Acute Respiratory Syndrome (SARS-CoV2)virus, which infected 2,078,605 people from 213 areas, countries and territories with 139,515deaths (table 1) till April 17,2020.Till date, there is no vaccine or effective measure to stop its spread [16]. Apart from analyzing the evolutionary aspect, the article also discusses the probable genetic variation leading to substantial uncontrolled health risk to human life [13, 14] causing a higher uncontrolled health risk to humans.

2. Evolution and future reappearance:

The viruses which contain RNA as their genetic material have potential to get evolved [21] and coronaviridae family has RNA as genetic material [22], which can evolve. In sequence, the viral genetic evolution has occurred in SARS-CoV that spreads through human to human contact [12] and this idea has been supported by [23]. They stated that SARS-CoV and SARS-CoV2 belong to a beta group of corona virus. They have 70% similarity at a genetic level showing DNA level differences among them (figure 1). This indicates that both viruses are 30% different in their genetic structure that is a result of mutations such as genetic recombination, gene deletion or insertion creating the probability of outbreak in future like its ancestors created in the past [16]. Likewise, genome level gene exchange, recombination [24], gene deletion or insertion may create a probability of outbreak in future, like past incidences [25] (figure 1) such as SARS CoV epidemics.

Additionally, SARS-CoV2 is considerably similar with SARS-CoV helping for predictions on occurred epidemic health disaster, and corona viruses may be responsible for outbreaks with variant mutations like previous one in upcoming years [13, 14, 25] (Figure 1). This suggests that both types of corona viruses are genetic variants.

Besides, SARS-CoV and SARS-CoV2 are similar for their severity. This idea was supported by Huang, C., et al., Chen, N., et al., Wang, D., et al., [27, 28, 29] who proposed that SARS-CoV2 severity mimicked with previously spread SARS-CoV and they also share same clinical features [30].

Table 1: Shows updated SARS-CoV2 infection status as on 17 April 2020 [26].

Sr. no.	Reported Cases/ Affected Regions	Number
1	Confirmed	2,078,605
2	Deaths	139,515
3	Number of Affected Countries, territories or areas	213

Chaolin Huang et al. [31] supported our concept and stated that corona viruses might lead to substantially more novel as well as severe zoonotic incidences.

Moreover, clinical characters of 2019-nCoV showed similarity with previously studied beta coronavirus infections [31]. Features showed by 2019-nCoV infections revealed some resemblance with SARS-CoV as well as MERS-CoV infections [32, 33].This strongly suggests that the novel coronavirus (SARS-V2) has evolved from previously observed SARS-CoV, a member of the betacorona virus group.

Additionally, there is a difference between SARS and 2019-nCoV regarding immunogenicity as former causes pulmonary inflammation with high level lung damage whereas the second causes raised production of Th2 cytokines retarding inflammation [34]. This effect might be due to 17% genetic variation caused by 2019-nCoV in PL pro sequences. As a result, the international crisis has occurred and there is no proper vaccine or drug against it till writing this article.

In spite of 83% similarity in the PLpro sequences of SARS-CoV and SARS-CoV-2, both of them share active sites which are similar [35]. According to Huang, C. et al. [27], infections by SARS-CoV-2 and earlier betacoronavirus showed similarities in clinical characteristics. To add, sequence identity between SARS-CoV2 and betacoronavirus members regarding domains of conserved replicase is lower than 90% [36] suggesting the relationship between both entities.

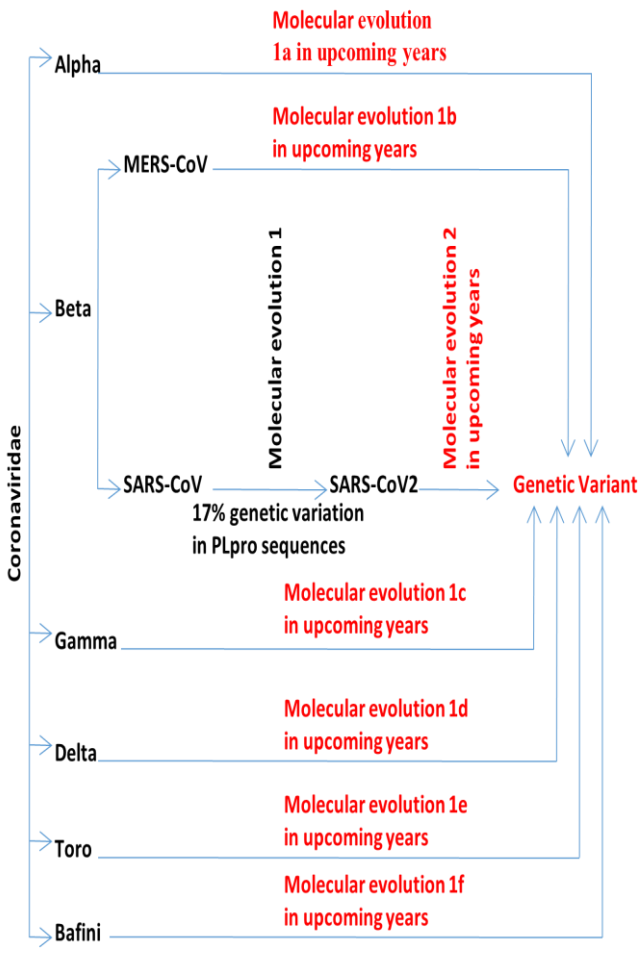

Figure 1: Schematic representation of the predicted evolution of Coronaviridae members with probable effects on human health. Note: 1a, 1b, 1c, 1d, 1e, 1f represent predicted evolutionary pathway of alpha, gamma, delta, toro and bafini viruses, respectively.

SARS-CoV-2 is considerably homologous to CoV that caused SARS (Severe Acute Respiratory Syndrome) during 2003. Also, SARS-CoV2 pathogen is more similar in relation with genetic makeup to SARS-CoV as compared with MERS-CoV [37, 38, 39]. As well, both have a common factor, i.e. human ACE2 receptor [39], which indicated that the genetic modifications in newly arrived pathogen do not affect human cell receptor recognition. With the exception, the COVID-19 pathogen binds human ACE2 more weakly with help of its S protein than SARS-CoV, causing less potential infection than SARS-CoV [37]. Furthermore, it was observed that death rate due to COVID-19 was found as 2% [40] while that of SARS spread in 2002, it was 10% [41] and in case of MERS, it was 37% [42]. It may be because of genetic modifications. Moreover, SARS-CoV has same size as SARS-CoV-2 [43], and both have high homology [44] supporting morphological similarity among them.

Interestingly, over 95% sequences show a similarity between SARS-CoV2 3CLpro and RdRp protease with that of SARS-CoV, and both viruses have 79% genetic similarity in their sequences [39]. Besides, they share potentially conserved Receptor Binding Domain (RBD) along with S protein domain [35,37,45] which is due to recombination/mutation acquisition in SARS-CoV-2 [16]. To add, novel viral host cell entry and replication proteins are similar with that of SARS-CoV with respect to their structure [46].

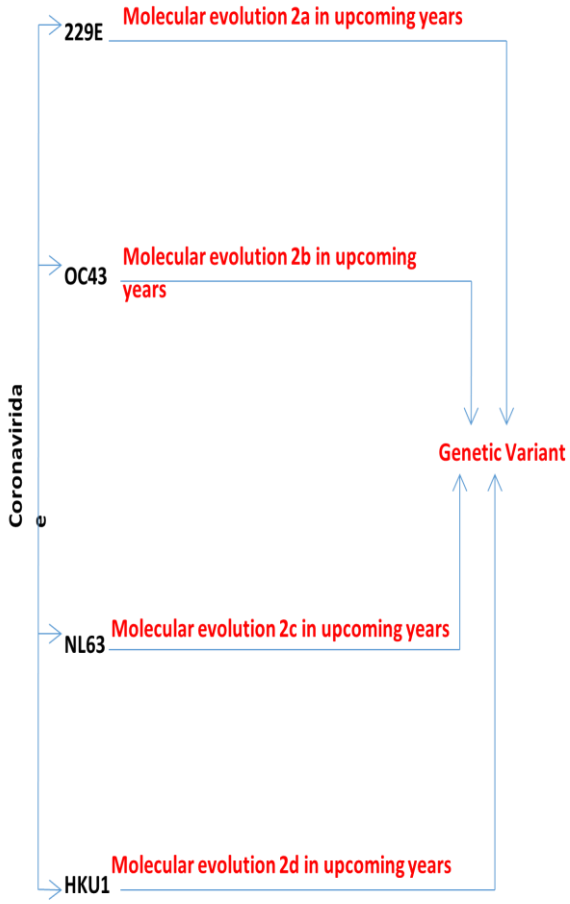

Figure 2: Schematic representation of the predicted evolution of Coronaviridae members with probable effects on human health. Note: 2a, 2b, 2c, 2d represent predicted evolutionary pathway of 229E, OC43, NL63, HKU1 viruses, respectively.

Additionally, it is found that SARS-CoV2 is one of the seven coronaviruses that infect human beings and others are MERS-CoV, SARS-CoV (cause severe infection), 229E, OC43, NL63, HKU1 (cause mild symptoms) [49]. In future, genetic variations may occur in the last four types (figure 2). Since the COVID-19 pathogen has similarity with SARS-CoV along with some symptoms, there is sense of its upcoming arrival [13, 14].

Out of six genera (ending with suffix 'virus') of family coronaviridae, i.e. alpha, beta, gamma delta

toro and bafini [20], betacoronaviruses include SARS-CoV, MERS, SARS-CoV-2 [46] and SARS-CoV-2 is a novel coronavirus in the genus that is belonging to MERS-CoV and SARS-CoV (figure 1). Like MERS-CoV and SARS-CoV, SARS-CoV2 targets lower part of the respiratory system leading to pneumonia and it also infects heart, kidney, gastrointenstinal system, liver as well as central nervous system [47, 48] showing pathological similarity. It means that the virus family understudy is genetically changeable and in upcoming decade, the same virus or other viruses of the same family will reappear [13, 14] with their genetic variants (figure 1).

3. Conclusion:

The coronavirus family is highly changing and its genetic variants may appear. In this sequence, genetic mutants of SARS-CoV2 may be detected in future.

Acknowledgement: Authors are thankful to Dr. Anant Shinde, Yashwantrao Chavan Arts and Science Mahavidyalaya, Mangrulpir, District Washim, Maharashtra, India for his support and motivation in writing this manuscript.

Authors' contributions: RD: Developed an idea and wrote the manuscript. AS: Verified the data. SB: Improved the manuscript. SW: Corrected the manuscript.

All authors read and approved the manuscript.

Competing interest: Authors declare that no conflict of interest exists among them.

Ethical statement: Since this is a review article, no ethical permission is required.

Grant Support Details:

The authors have not received funding for this work from any agency.

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Cite this article as: Dhakane R, Shinde A, Bhattacharjee S, Wagh S. Can Coronaviridae Viruses Reappear with their Novel Variants in Upcoming Years? Int. J. Micro. Sci.. 2020;1(1):1-6.