

Editorial

Sars CoV2 - How Challenging is the Emerging Variant?

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Sars CoV2 (Novel Corona Virus), is soon emerging as the mother of all pandemics in respect to the number of cases, that hovers over 146 million.^{1,2} As of 24/04/2021, India recorded over 16.6 million COVID cases with 189,549 deaths, second only to the United States of America (USA) with the corresponding figures at 32,735,704 and 585,075 respectively.² Officially the days are not far away, when, India will take away this unfortunate and infamous crown from the USA, especially, the way the pandemic has flared up in its' second wave. But estimates based on the number of the population tested per million, it is being predicted that India is harbouring about 400 million cases, more than the total population of USA.³

Way back on 17 Apr 2020, almost a year ahead of the present situation, Moore J. predicted that the world will be worst hit by the second wave of Sars CoV2, which was highlighted by Mishra et al. in their article 'Pandemic Dynamics, the three Waves of COVID-19 and the Way Ahead'.^{4,5}

This, unfortunately, seems to have come true. The rampage caused by the nationwide 2nd wave in India is its elucidatory testimony. Though many players have led to the present scenario, the most important and challenging ones are the emergence of mutant strains of the virus, namely, Variant of Concerns (VOC) and Variant of Interest (VOI) which has severely incapacitated its management.

Genetic mutation is an inherent property of evolution. Viruses, the tiniest form of living creatures, are no exceptions. The more immature they are, the more severe and rampant is the process. According to the Baltimore classification of viruses that takes into account the genetic material contained in the virion, we have a host of viruses that ranges from the simplest positive-strand (ss+) RNA viruses like human rhinoviruses, coronaviruses, polioviruses and hepatitis C virus to more complex double-stranded (ds) DNA viruses like papillomaviruses and herpes viruses.⁶

The rules of thumb states "The more primitive and simpler the genetic contain the more aggressive is the mutation"! The frequency of mutation is dependent on virion infected cell cycle, the novelty of the virus and its infectivity rate. Primitive genetic material, short cell cycle, virgin population (novel virus) and higher R nought (spread/infectivity) all

favour rapid mutation. Unfortunately, as of today; all these factors are in favour of SARS-CoV-2.

While most mutations are nonconsequential and some even act against the replicating virion, but still some mutations do it a favour in terms of fitness advantages. These fit lineages as experienced with an Asp614Gly spike substitution in the UK (alpha) variant B.1.1.7, The P1 Brazilian (gamma) variant with mutations compared to the B.1.1.28 lineage, the Glu484Lys substitution in the South African (beta) variant 501Y.V2 (B.1.351), and the Californian variants with mutations at B.1.427 and B.1.429 have become the sources of concern (VOC) as they have turned out to be more contagious and can evade (at least to some extent) the existing therapeutics including vaccines.^{7,8}

The plight does not stop here. As more genomic laboratories across the globe become proactive in carrying forward the genomic sequencing and sharing their reports at global forums like the Global Initiative on Sharing All Influenza Data (GISAID), National Centre for Biotechnology Information (NCBI), the European Molecular Biology Laboratory's European Bioinformatics Institute (EMBL-EBI), and the DNA Data Bank of Japan (DDBJ); the ugly face of the evolving virus is getting clearer.⁹

CDC has rightfully categorized them into three main groups namely, VOI, VOC and VOHC (Variant of High Consequence). Though at present we don't have a VOHC for Sars CoV2, the emergence of VOIs and VOCs are getting rapidly reported. Some of the examples of VOIs doing the round are the B.1.526, B.1.526.1, B.1.525, and P.2 and B.1.617 (Indian variant).^{10,11} As of 03/05/2021 - 1,339,711 hCoV-19 data have been shared via GISAID12.

The VOIs may be the potential candidates to upgrade them to the next stage i.e., VOCs. The basic differences between them are, VOIs have qualities like carrying specific genetic markers that in all probability will affect virus transmissibility, prompt the virus for immune escape, and challenge the existing diagnostics and therapeutics modalities along with the evidence that it has contributed to recent increased in the proportion of cases or has led to a unique outbreak. VOCs are those who have evidence-based qualities that link them to influencing/impacting existing established diagnostics through widespread interference with diagnostic test targets along with reduced therapeutic and vaccine response. They too are associated with either increased transmissibility or disease severity or both of them. The VOC lineages are also reported to replace the previous ones (variants) thereby enhancing its public health complexities.¹⁰

Like their properties and presentations, their containment too asks for different but somewhat overlapping approaches. They include boosted genetic sequence surveillance,

improved laboratory categorization, and epidemiological investigations to have an insight into the swiftness of the viral spread, its ability to influence disease severity, treatment and vaccine efficacy. VOC in addition mandates reporting to WHO (World Health Organization), CDC and initiation of local and regional efforts for its' containment by increased testing, development of new vaccine variants, therapeutics agents, along with the special emphasis on strengthening health infrastructure, health care supplies and trained manpower.

While building on these essentials, the basics of pandemic containment should not be lax, as noticed on multiple occasions by countries of all sects. Stricter epidemiological and genomic vigilance and geographical containment action are needed to prevent the evolution of further harmful VOCs that often associates with rapid transmissibility. Fast-tracking immunization activities, expanding its population coverage in terms of number and age group, employing/licencing multiple vaccines in immunization drives (cafeteria approach), along with the constant emphasis on the non-pharmacological intervention like double/ triple masking, social distancing, early imposition of travel restriction/ban from and to red flagged areas/countries and hand and environmental hygiene measures can play a lead role.^{13,14}

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