Remdesivir, Favipiravir, Dexamethasone and SARS CoV-2 Mass Vaccination Linked to Variants of Interest and Concern: Should We be Concerned?

Short title

What countries where SARS CoV-2 variants of concern and interest first evolved share in common?

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Key points:

SARS CoV-2 mass vaccination might help in evolution of SARS CoV-2 variants of concern and interest

Remdesivir, Favipiravir and Dexamethasone abuse might share in SARS CoV-2 variants of concern and interest evolution

We suggest that molnupiravir, if approved, would be least likely to benefit COVID-19 outpatients and might also share in evolution of these variants

Numerous SARS CoV-2 variants were suggested to cause a higher number of infections, worse clinical outcomes, escape of the immune system and vaccines as well as diagnostic hardships[1] and the WHO has suggested a preliminary evidence of their more rapid spread, more severe complications or evasion of previously acquired immunity [https://www.nature.com/articles/d41586-021-01274-7] and they were dubbed as variants of interest or concern [https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-info.html#Consequence]. Thus, we wish to analyze some potential causes that might have triggered and/or will trigger the evolution of these virulent variants while exploring the recent Indian crisis.

We have witnessed the emergence of the SARS CoV-2 B.1.617 variants first identified in India in October 2020 and later the delta B.1.617.2 variant of concern was identified in more than 96 countries as recently declared by WHO experts [https://www.who.int/emergencies/diseases/novel-coronavirus-2019/media-resources/science-in-5/episode-45---delta-variant]. Notably, the Indian surge of cases and mortalities was considered of international grave concern [https://www.nature.com/articles/d41586-021-01274-7] especially as these variants, including B.1.617.2 , were expected and later are shown to be the most dominant ones elsewhere [https://www.cnbc.com/2021/06/16/who-says-delta-covid-variant-has-now-spread-to-80-countries-and-it-keeps-mutating.html].

Some authors have claimed that SARS CoV-2 B.1.617 variants have mainly evolved first in India because of lack of control on crowd-gatherings [https://www.nature.com/articles/d41586-021-01059-y] and others suggested that its spread might have been prevented if strictest quarantine requirements were imposed on everyone arriving from India [https://www.nbcnews.com/news/world/u-k-records-over-10-000-covid-cases-first-time-n1271197?fbclid=IwAR1dsQzKBFuKeBihy9aQ-olJZh4wA67YhXmRFesPMP3UctwhmRIYeSqAlc4].

However, we suggest that these theories are least likely probabilities as many developing countries impose similar or much worse minimal control on crowd-gatherings, yet their report of SARS CoV-2 variants and more importantly their surge of COVID-19 infections and/or mortalities are much better than that of India though some of these countries share

similar genetic profile. Meanwhile, we claim that not only the delta variant but almost all other previously discovered as well as the anticipated upcoming variants have evolved simultaneously in different countries [https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/], though detected first in some and named after them; British, South African, Brazilian …etc and we postulate that most of these countries share some of the following favorable variant-genesis conditions/elements.

The first mutual condition/element in these countries is the prevalent use of the ineffective and mutagenic antiviral drugs; remdesivir and favipriavir, respectively [2] especially in combination with the immunosuppressive dexamethasone[3] and we consider the abuse of these drugs as a main cause of evolution of some or all of these SARS CoV-2 variants of interest and/or concern. Moreover, we anticipate that the Indian crisis that led to unprecedent surge of COVID-19 induced mortality might be repeated, in any other country, with potentially more virulent or transmissible variants e.g. delta plus and lambda especially after the end of the progressive mass vaccination programs with SARS CoV-2 vaccines[4] which we consider the second mutual condition in these countries.

We recommend, a prompt decision to discontinue remdesivir and favipiravir use in COVID-19 management is being made together with a re-evaluation of the short and long-term efficacy/hazards aspects of the current SARS CoV-2 mass vaccination programs which might soon reveal as one of the worst medical decisions that have ever been made as it should have been only considered to be administered to the high risk groups, and probably the subunit rather than the gene based or the inactivated ones, after an informed personalized evaluation of the risk/benefit ratio has been undertaken[5].

Moreover, we suggest that the anticipated mutagenic antiviral drug molnupiravir[6] would not significantly differ from favipiravir[7]. However, we anticipate a remdesivir-like false "announced success" in outpatient settings after the overt failure to manage the COVID-19 hospitalized patients while providing subtle excuses [https://www.reuters.com/business/healthcare-pharmaceuticals/merck-plans-large-outpatient-trial-covid-19-pill-stops-study-hospitalized-2021-04-15/] and unfortunately when billions of dollars are on the stake [https://www.yahoo.com/gma/merck-signs-1-2-billion-175655042.html], few might dare to argue that the risk benefit ratio of using

molnupiravir for COVID-19 outpatient settings is totally imbalanced with more profound short (evolution of variants of interest and concern) and long (potential latent carcinogenicity) [2] risks to be considered.

Finally, the need of a proper COVID-19 management protocol has been shown of paramount importance to reduce the probability of resistant strain establishment[8] and we suggest that our immunomodulatory safe, simple, inexpensive and successful one that has been unfortunately ignored for more than one year might prove the best suitable alternative to save lives and to minimized the evolutionary risk to develop more virulent and lethal SARS CoV-2 variants[9] [10].

Funding

None

Competing interests

None

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