Letter to the Editor

Remdesivir, Favipiravir and Dexamethasone Linked to SARS CoV-2 Variants of Interest and Concern: Could SARS CoV-2 Mass Vaccination Programs and Molnupiravir Add Oil to The Fire?

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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 80 countries as recently declared by the WHO. 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 are expected and shown to be the dominant ones elsewhere over time [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 variants

have evolved simultaneously in different countries, though detected first in some and named after them; British, South African, Brazilian …etc.

We postulate that the prevalent use of the ineffective and mutagenic antiviral drugs; remdesivir and favipriavir, respectively [2] especially in combination with the immunosuppressive dexamethasone[3] are the main causes of evolution of these SARS CoV-2 variants of interest and/or concern leading to the recently encountered Indian unprecedented surge of COVID-19 induced mortality. Moreover, we anticipate that the Indian crisis might be repeated, in any other country, with potentially more virulent variants e.g. delta plus especially after the end of the mass vaccination programs with SARS CoV-2 vaccines[4] unless, as 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, probably the subunit not 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].

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Competing interests

None

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