A Viewpoint Commentary

Buffalo as a New Model for Long COVID-19 Study and for Recovering the SARS CoV-2 Polyclonal Neutralizing Antibody, Using an Online Affinity Column Adsorption Technology, for Therapeutic Interventional Modality in Humans: A New Multi-Purpose COVID Research Proposal

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Since WHO mentions the pandemic nature of Covid-19 infection, we are witnessing almost 100 million cases and almost over 2 million deaths due to SARS-CoV-2 infection, causing enormous economic devastation on a global scale. Today, when it comes to tackling the immunity against this deadly virus, all the global scientific community are coming together, persuing with rigor all research and development strategies into the identification of the genetic variations of CoV-2; host response to virus variants; and antivirals and vaccines immunotherapy, where the use of Artificial Intelligence [AI] tools in large data and pattern analyses proved to be of enormous help that we could not do without [1].

Previously in a series of collaborative studies, as a team, we highlighted the benefit of vaccines as the main clinical intervention, and we made some new proposals on some alternative immunotherapy and addressing some matters of concern on the safety/ efficacy aspects of the current interventional therapies [2-7], with the main objective of stimulating some newer ideas and proposals to hasten a solution to defeat this worldwide disease.

In any infectious diseases such as Covid-19, animal studies help scientists predict how well a candidate vaccine will work. They inform scientists which immune cells triggered by the vaccine are protective, whether the vaccine will be viable as human intervention, and how the disease progresses in individuals with long Covid and in compromised immune systems. In the current proposal, the focus is on the use of buffalo and other animals as the essential clinical safety efficacy requirements of any interventional therapy and in the production of polyclonal antibodies against CoV-2, as new research proposals are highlighted.

The rhesus macaque, a monkey widely prevalent in India, might prove to be a promising model for vaccines induced polyclonal neutralizing antibodies against Covid-19. Another useful alternative, even as a better choice for the large scale production of such antibodies, is baboon with a greater infective disease development potential, making it a useful candidate for evaluating antiviral therapeutics and comorbidities as an essential requirement of phase II clinical trials for Cov-2 vaccine for approval [6].

The concept of using the buffalo and some other non-human primate species [i.e., the Indian rhesus macaque; African baboons and common marmosets as the new-world origin and some young and old animals], to be infected with CoV-2 to investigate the protective immune responses that might be produced with a vaccine would be highly relevant, as the response of a human to this infection appears to be intriguingly quite different and appears to be age-dependent. For example: some, mostly the young population, never noticed that they are infected with no symptoms at all; some asymptomatic and mostly the young populations; some with long COVID with general long term fatigue potentially due to developing autoantibodies that circulate for a very long time [7]; and some with very acute and severe diseases often in the older population, with fatal outcome [3-7].

Intriguingly the nature of the above old age related mortality that we were witnessing in the context of CoV-

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2 normal strain is now shifting to younger individuals with the appearance of newer deadly variants that spread even faster in younger populations, often requiring emergency hospitalization, in some local areas in the UK [i.e., Kent and London, Manchester, etc.], as indicated by the continual statistical analysis, followed by genetic fingerprinting surveillance of the dialogistic samples [2]. More recently, newer variants such as those seen in the South African younger population and the most fearful Brazilian types that can even re-infect some individuals who have already recovered from different Covid strains, are coming to the surface in the UK, and there are some concerns about whether the current vaccines would be effective on these fast-spreading variants [3].

In the non-human primate immune system, as compared to human, there are some signs of acute viral infection do occur, leading to pneumonia; hence it is worthy of exploring whether, like human cases, a strong response in both antibodies against Covid spike after the two weeks and also immune responses will develop to clear this antigenic marker of Covid infection. Nevertheless, so far, such a study using some large candidate animal of all age ranges to study changes associated with the immune system is missing, and this will be warranted to be persued in view of a shortage in the current supply of all vaccines and the recently reported concerns in the development of blood clot in the lung with the use of some of the current vaccine in use in some European countries.

However, according to ISTH, it is not clear that the clot formation is due to vaccination or coincidental. Hence this provides another new opportunity for a new research trial through the relevant animal study, as the infection itself is associated with complements activation and cytokine storms leading to thromboembolism and organ injuries, as described previously [4-7].

As we have indicated previously [4-6], another highly fruitful proposal is the use of some existing online affinity column adsorption technology that can successfully remove the circulating specific polyclonal Covid neutralizing antibody as a hyper concentrate [4-6]. This well-established procedure if fully applicable to this study to produce purified virally inactivate Covid neutralizing antibodies for immediate applications directly for creating passive immunity in humans or primate, even as a booster for the current vaccine, as some vaccines have lower efficiency and take about 3 weeks to produce a relevant standardized level of antibodies. This work can be carried out in collaboration with experts in the field of modern affinity column and the blood purification methodology, with good clinical and therapeutic experiences that are continuously improving.

2021 is called by many the year of unwanted CoV-2 variants as the unwanted gifts are still creating chaos all over the world. Hopefully, in 2022 this Buffalo project will bring some newer opportunities even as a small step forward to deal with serious unresolved challenges that this infection has brought about and still tests human ingenuity to beat off or at least to survive the Covid variants that are still developing fast and are creating both health and economical chaos.

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