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Commentaries

A roundup trends analysis of CoV-2 alpha to delta variants that are edging race against the current vaccines in use: back to basic cautionary measures with higher rate of vaccination to all susceptible individuals including children and vaccine hesitant groups and using targeted booster vaccines and alternative therapy based on NAB concentrates with direct immediate clinical impacts

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This invited viewpoint commentary, in the from of a multimedia activities content in concert with some personal inputs on some of opinions expressed based on my earlier publications are designed to fill some of the unmet needs of the medical community by reporting information pertaining to clinically relevant development i CoV-2 variants , stipulating the editorial independence of this author.

The revolutionary advancements in genomics have engendered considerable Interest in many complex fields of diseases including the better characterization of the emergence and treating CoV-2 mutated viral infection strains, holding significant promise in providing clinical benefit to patients, where there are a variety of challenges need to be addressed when developing Immunotherapy: Choice of modality; Mechanism of action and the Safety / efficacy studies to bring the therapy to clinical trials that need to be explored in line with the regulatory paths to bring these modalities to patients.

Current studies on how CoV-2 proteins interact with endogenous human proteins are critical to gain deeper understanding of the virus's mechanism of action and to identify potential candidates for its effective therapeutic targeting. The ability of CoV-2 variants proteins to either form plasma membrane ion channels or alter the function of the epithelial sodium channel and the α3β4 nicotinic acetylcholine receptor utilizing a variety of approaches demonstrate that CoV-2 proteins, specifically E and S proteins altered the function of human plasma membrane sodium ion channels regulation, however the exact mechanisms underlying those observations still to be determined.

In this context Our current understanding of the B.1.617 lineage of CoV-2, especially the delta strain B.1.617.2 that has contributed to the new wave of infection in the native poorly [about 2%] vaccinated Indian subcontinent that lucking the natural immunity to this variant is rather incomplete. But based on the unique UK' genetic finger printing surveillance analysis and recent structural and serological analyses, using artificial intelligence tools, it appears that even individuals previously infected with either the UK B.1.617 (alpha); South African B.1.351 (beta); or Brazilian P.1 (gamma) variants are likely to be susceptible to reinfection by the Indian B.6.172.2 (delta) strains and the current vaccines only provide some partial protection against these variants that are antigenically divergent.

In fact current trends analysis in the UK suggest delta variant accounts for 90% of new CoV-2 variants cases and it is about 60% more transmissible than the alpha variant, and might also become linked to a greater risk of hospitalization, as it is somewhat more resistant to vaccines [i.e. by less than 20% after one dose and 4% to two doses] and today almost150.000 tested positive with delta variant in the UK, where 2/3 adults are vaccinated with two types of classical approved vaccines. This is the problem with all types of vaccines, including the new one dose vaccine, until we got something near a population immunity threshold against all mutated variants with a much higher coverage to protection

against a newly emerging variant and to keep cases down, at the same time with the faster rolling out the newer type of vaccines to create herd immunity against not only against the spike proteins but the whole structure of virus that undergo continual changes in shape, size and charge, should also be taken into consideration.

Moreover we must always keep in mind that no vaccine is 100% efficacious and there will be always some poor and non -responders to all vaccines some more than others. In fact in USA when in a non-responder to Pfizer vaccine, was treated with one dose Janssen one dose vaccine, after 20 days, enormous rise in antibody observed supporting the values of mixed matched combination vaccines. No wonder that some targeted multi-variants vaccines are in the planning stages and some alternative therapies- that have been recently proposed by this author to optimize safety efficacy and minimizing the potential toxicity of earlier proposed convalescent neutralising antibodies as concentrate [NABC], obtainable as new bioproduct by affinity column or designated beads, from mini pools of convalescent plasma and successful vaccinated Individuals timely -should be brought forward for direct booster therapy, following clinical trials.

What we need most right now is a real culture change to survive or even beat covid, although the long covid that is estimated to stay in some individuals for more than 6 months remains an unresolved problem. Therefore the calls for added caution is most warranted, in particular at a time when current research indicate that in France, in our close shore, the South African beta variant is also reaching up to 20% while its spread in the UK still remained below o.1%, firmly indicating some added cautionary protection measures must be in place as this variant can potentially spread to UK and this virus with multiple variants continue edging race even the against the current vaccines in use in the favour of variants with devastating outcome already in home care units and so on .

The ideal scenario is that we build our targeted multi-variant vaccines and the alternative therapy wall before we get exposed to emerging CoV-2 variants and this means that even if one do get an outbreak, we get sufficiently few people that are susceptible, with the reproduction number [R] never gets above one, as the sign of an increase in that outbreak. The problem is that we haven't reached that protective level yet, and so if we do get new variants and the numbers of cases growing there are plenty of susceptible people to pass the infection on including the children and vaccine hesitant individuals all over the world. This apparently is twice higher [40%] in France than in the UK being about 20%. Therefore it is time that we must go for full belt and braces approaches all the way to stop additional sources of imported variants – we can't ignore either school children, pregnancy and /or predominately vaccine hesitant youngsters in vaccination campaigns, If we do, then we could end up in a new cycle of variants. In another words there is no point leaving it half done as evidence is accumulating the early toxic effects this infection is becoming apparent in youngsters who upon delta variant infection are developing lungs, Intestines, kidneys and Organ damages, often leading to death, even in the younger healthy age.

Another important issue that deserve more attention is that in this infection, in particular the elevated levels of blood neutrophils appear to predict severe respiratory disease often leading to unfavourable outcomes. Neutrophil-derived extracellular traps (NETOSIS) play a pathogenic role in many thrombo-inflammatory states including sepsis, thrombosis, and respiratory failure. NETOSIS are extracellular webs of chromatin and microbicidal proteins that are an evolutionarily conserved aspect of innate immune host defence systems and also having potential to initiate and propagate inflammation and thrombosis. Thrombosis and activation of neutrophils are bystanders of a CoV-2 infection in humans. Hence while the early-phase thrombi formations are platelet rich clot, but the late-phase thrombis are associated with neutrophil activation and NETOSIS. Intriguingly some vaccines, that are not an infective agent do appear to obey a similar mechanism, as some very rare events of vaccine induced thrombotic thrombocytopenia [VITTP], a rare phenomenon predominately observed in young female under the age of below 30, with possible host predisposition [on average one per million cases] have been previously highlighted for some types of vaccine. Hence targeting specific thrombotic events during the infection might help in remedial action to ameliorate potential platelet rich clot in the brain and lung tissue and the other organs damages.

Unfortunately, despite this bleak scenario the UK Government is keeping the promise of the call the 19th July as the freedom day and opening all the flood gates infections free for all without any mask, even the overcrowded areas with poor ventilation including some bars and night clubs for youngster with self-restriction impulses without any imposed compulsion. No lesson learnt yet even from either Israel where the full vaccination gave false sense of security and by removing the imposed restriction now children having it or from our even more close neighbours with advance vaccination policy, the Netherlands where 5 % rise in infection observed and more importantly that devastating delta variant infection is still exponentially rising locally in the UK and we have not seen the peak yet.

Easy going in removing the restriction in moderation is the strategy that we need to be followed in the race with these variants while the issue the prolonged mild long COVID still require more economical and R& D investments. Interestingly evidence is accumulating that in all twenty of Long- COVID patients who received neuromodulator treatments reportedly had significant improvements in their symptoms in just 14 days news worthy item right now to be explored further. In more severe cases meanwhile we still need a radical approach to address the sustainability of some newer booster alternative therapy, so be if it come from mini pools of cadaveric serum of patients whose antibodies could not help them to survive Covid and this should be prepared by trusted manufacturers under the c GMP compliance.

To sum up to date, the viral pandemic has resulted in millions of infections worldwide. This virus, with its ever changing multi-variants' nature is still causing the most devastating death in innocents individuals despite considerable progress in large scale vaccination programme and in a foreseeable manner internationally, following the slogan that "No one is safe until everyone is safe".

We will never be justify rationally if the international community not coming together as a team acting together with

the hope to live in harmony with vigilant, pre-empting such as axis of evil running through before they cause further damages, even if it required more sacrifices and making newer tools to be available for use that is the logic legitimacy of any war on terrors. Living with Covid means we must go along with the concept of having '' less fear & more hope'' with plenty of more perseverance.

Technologies also deserve to force re- examination and their justness in the use of target- specific move and enabling the avoidance on non-toxicological outcomes. The reality of course is rather more complex as belligerents can end up causing more harm, as nothing is pure and simple. Moreover just the use of technologies and artificial intelligence decision making complicates the idea of the subject of vaccination the objectives being the targeted recipients with enormous individuals' variability being human consequently it is very difficult to invoke a rational criteria with explicitly that we no longer upholding our own day.

In short CoV-2 variants of the current concerns are more infectious and can evade pre-existing immune responses hence Investigating immune responses against alpha Beta, gamma and delta variants with some recombinant spike antigens must be kept in sight in future COVID-19 research regarding applications in other haematological malignancies where the focus remains on the benefits and risks of currently available therapies for some acute lymphoblastic leukaemia, lymphoma and multiple myeloma where special focus will be placed on the advantages and disadvantages of bispecific antibodies vs. cellular therapies including T cells, NK cells and transplant strategies.

Needless to mention that last year scientist from around the world undertook genetic analysis to uncover the genetic factors influencing why some Covid patients develop severe, life threatening disease, requiring hospitalization, while other escape with mild symptoms or none at all as it has been revealed that 13 loci, or location in the human genome, that are strongly associated with infection or severe covid variants. The mother virus is saying you need some more innovative idea even to come close to compete with me for this race. Your vaccines are not even making a sense just a plain white cup and saucer as an enigma in its directness of encountering it, haunting for some and commanding masterpiece in its destination in itself that we pay attention to the detail of our lives.

The challenges of looking ahead to the significance and sustainable future, while exploring the benefit and boundaries of working together while Covid still going strong after racing around the world and still winning is amazing experience. Living with covid is more than living with a regular cold infective viral infection it's all about the care givers looking to give life to those struggling to survive and engaging youngsters to joining the sacrifices by all with due perseverance. No country alone can resolve the pandemic and team working is the only way out in such natural pandemic biodiversity. Here again a lesson to be learned from India, where delta variant begun as today by targeting their locally produced vaccines to their community most in need managed to vaccinated one third of their huge adult populations timely and reached even some villages, by food in 3 hours and vaccinated almost 80% of them despite being mostly vaccine hesitant individuals, with success, clearly reflecting that perseverance do pay.

Cite this article

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