Review of: "Factors influencing variable symptoms of COVID-19 patients and proposed revision of public policy for COVID-19 vaccination"

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The title of the paper: “Factors influencing variable symptoms of COVID-19 patients and proposed revision of public policy for COVID-19 vaccination implies a full analysis of all of the influencing factors” is a bit misleading. The author only focuses on the individual’s viral susceptibility and immune response based upon the person’s genetic profile. Overlooking other important influencing variables.

Therefore, as it stands, it would have to be rejected. However, I believe the topic itself is so important that the author should not give up, but to encompass the additional factors, so that the final product is a lot more comprehensive. More importantly, is accurately reflecting the title of the paper.

I have also made a few specific points to consider:

Page 2 paragraph 1, lines 7 to 11: In the paper it is stated: “However, records show that the new viral strain, SARS-CoV-2 (O-Micron) and many others still cause a similar ratio of asymptomatic cases, severe cases and mortality as the original strain of SARS CoV-2.” However, the records showing this are not referenced. Our numbers show that the omicron variant although more infectious, is extremely mind when it comes to severe cases and mortality compared with the Wuhan variant. I agree that immune evasion to explain the cause of pathogenicity is an important factor, it is a mystery, and I’m you would appreciate, a very complex one. From our government figures it is mostly the older people who died (80% over the age of 70, as from May 30, 2023). If the major factor was genetic susceptibility death toll would been similar across all age groups. Therefore, it would appear that age is a major factor. Also, it may be the effectiveness of the vaccine itself.

Thailand has 7 vaccines that are approved with another 12 in clinical trials:
https://covid19.trackvaccines.org/country/thailand/

Also, the current mRNA vaccines are not effective against the later variants:
Statement from CDC Director Rochelle P. Walensky, MD, MPH on Today’s MMWR. Aug 2021

https://www.cdc.gov/media/releases/2021/s0730-mmwr-covid-19.html

The 7 vaccines utilise different technologies eg. SinoPharm and SinoVac utilises the whole virus which has been inactivated. Essentially a traditional vaccine. These differences may explain, at least in part why some vaccinated people do not get infected.

Page 2 paragraph 2, lines 7 to 9: The author refers to previous report (references 16 to 18). In the conclusion section of reference 16 it states: “At this time, it is not clear whether the structure and function modulation of ACE2 in different variants could have a role in the probability of the infection or not. There are contradictory results for the impact of ACE2 variants in COVID-19 severity.” What may be a more significant factor is the up-regulation of ACE2 in the lungs as a result of smoking and/or lung disease (e.g., COPD). Again, does ACE2 in the lungs increase with age?

Page 3 paragraph 3, lines 1 to 3: In the paper it states: “The best strategy for the antibody to neutralise the viral agent is to bind the viral RBD. This is the main approach for manufacturing the viral vaccine.” Apart from the Chinese vaccines that using the whole virus, all of the others are using gene therapy technology to produce in-vivo part of the viral spike protein which binds to ACE2. The problem with that is that the virus is continuously mutating, and there comes a point when a new variant is formed which can still bind to ACE2, but effectively evades the vaccine which then infects to next person. I cannot think of any former vaccine using gene technology that has been shown to be effective against a virus to date. Also, there is far more to the immune system than just antibody binding. Which is why naturally acquired immunity is superior to acquiring immunity via., a vaccine.

Page 5: I agree with the statement regarding Group 6. However, there are some antivirals that have been approved and shown to be effective to varying degrees, such as Remdesivir, Paxlovid, and Molnupiravir. Ivermectin, and fluvoxamine for the treatment of COVID-19 has also been allowed for use in many counties of the world, and extensively discouraged by others.

Page 6 paragraph 1, lines 3 to 9: The author makes a blanket statement in the conclusion: “Based on this aspect, everybody should be vaccinated since we do not know who does (or does not) have susceptibility viral receptor/co-receptors and it is too complicated to identify the cellular variants for every individual.” I would like the author to consider some of the issues regarding such a statement. The author needs to research whether or not the vaccines are safe and effective and determine the risk/benefit of vaccinating everybody. Some references to consider:

1. Outbreak of SARS-CoV-2 Infections, Including COVID-19 Vaccine Breakthrough Infections, Associated with Large Public Gatherings — Barnstable County, Massachusetts, July 2021. US Department of Health and Human Services/Centers for Disease Control and Prevention MMWR / August 6, 2021 / Vol. 70 / No. 31
2. Statement from CDC Director Rochelle P. Walensky, MD, MPH on Today’s MMWR. https://www.cdc.gov/media/releases/2021/s0730-mmwr-covid-19.html
3. `Trends in Disease Severity and Health Care Utilization During the Early Omicron Variant Period Compared with Previous SARS-CoV-2 High Transmission Periods — United States, December 2020–January 2022. US Department of Health and Human Services/Centers for Disease Control and Prevention MMWR / January 28, 2022 / Vol. 71 / No. 4

4. `https://www.openvaers.com/covid-data
5. Gao et al., “Extended SARS-CoV-2 RBD booster vaccination induces humoral and cellular immune tolerance in mice.” iScience 25, 105479 December 22, 2022 ª 2022. https://doi.org/10.1016/j.isci.2022.105479
6. Irrgang, Pascal et al. “Class switch toward noninflammatory, spike-specific IgG4 antibodies after repeated SARS-CoV-2 mRNA vaccination.” Science immunology vol. 8,79 (2023): eade2798. doi:10.1126/sciimmunol.ade2798

There doesn’t seem to be given any consideration to people who are already immune due to natural acquired immunity. It is immunity that counts, not vaccination per say. Some references to consider:

1. Gazit, Sivan et al. “Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Naturally Acquired Immunity versus Vaccine-induced Immunity, Reinfections versus Breakthrough Infections: A Retrospective Cohort Study.” Clinical infectious diseases : an official publication of the Infectious Diseases Society of America vol. 75,1 (2022): e545-e551. doi:10.1093/cid/ciac262
2. Yahi, Nouara et al. “Infection-enhancing anti-SARS-CoV-2 antibodies recognize both the original Wuhan/D614G strain and Delta variants. A potential risk for mass vaccination?” The Journal of infection vol. 83,5 (2021): 607-635. doi:10.1016/j.jinf.2021.08.010
3. Le Bert, Nina et al. “SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls.” Nature vol. 584,7821 (2020): 457-462. doi:10.1038/s41586-020-2550-z
4. Liu, Lihong et al. “Potent neutralizing antibodies against multiple epitopes on SARS-CoV-2 spike.” Nature vol. 584,7821 (2020): 450-456. doi:10.1038/s41586-020-2571-7
5. Block J. Vaccinating people who have had covid-19: why doesn't natural immunity count in the US? BMJ. 2021 Sep 13;374:n2101. doi: 10.1136/bmj.n2101. Erratum in: BMJ. 2021 Sep 15;374:n2272. PMID: 34518194.

As far as using data to govern policy. People who are genetically immune compromised, may not require a genetic test. Perhaps a past medical history may give a good indication (prone to multiple infections etc.). Such people could then be tested genetically as a confirmation. Different countries in the world have developed their own respective polices, I’ve provided links to a couple of examples:

https://www.folkhalsomyndigheten.se/the-public-health-agency-of-sweden/communicable-disease-control/covid-19/vaccination-against-covid-19/order-of-priority-for-covid-19-vaccine/

https://www.swissinfo.ch/eng/society/covid-19_coronavirus--the-situation-in-switzerland/45592192

Every country seems to have adopted its own policy moving forward perhaps Thailand’s policy will be different based upon a multitude of factor that have to be taken into consideration prior to implementing any form of action. I went to the WHO website to find out any information specific to Thailand: https://covid19.who.int/region/searo/country/th

However, further demographic information is required to determine the factors influencing variable symptoms of COVID-19 patients and proposed revision of public policy for COVID-19 vaccination