COVID-19 Vaccine for Elderly: Should We Be Reactive or Proactive?

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It has been a year since the Indonesian Government has announced its first COVID-19 identified in Jakarta. Since then, there have been more than 900,000 cases in Indonesia with case fatality rate (CFR) of 2,9%.[1] The number of new cases per day is now ranging from 9,000 cases to almost 13,000 cases. Not only in Indonesia, but the number of new cases along with the mortality rate in other countries, such as Malaysia, Japan, United States, and Europe region also increased dramatically.

COVID-19 vaccines are being investigated and the world hopes that vaccines will be the answer to tackle this pandemic. Is it really so? Immunization is an effort to induce immunity in individuals to prevent a disease or the complication related to the diseases that may be catastrophic. Immunization can be divided into passive, which is by giving certain type of antibody and active, which means that either we get the disease, or we get the antigen injected into our body.[2] Vaccination was first known in 1976, when Edward Jenner first injected a variola vaccine to a boy in order to prevent the boy from getting variola infection.[3]

Seroconversion and seroprotection are related keywords in vaccination. Seroconversion refers to specific antibody enhancement after active immunization by giving the vaccination, while seroprotection refers to the level of antibody to protect the person.[4] World Health Organization (WHO) stated that in order to decrease 50% of the risk of getting the infection, a vaccine must have a minimum efficacy of 50%.[4] Efficacy is the performance of the intervention (e.g. a vaccine) under ideal and controlled circumstances, which happened during a clinical trial. On the other hand, we also know the term of "effectiveness", which is the real performance of the intervention in real-world condition, which happened when we administer the vaccine to the individuals in the community with different baseline characteristics.[5]

Eradicating of a disease and/or achieving herd immunity are the main goals of vaccination, such as eradication of Polio by giving Polio vaccination. Herd immunity is a form of indirect protection from infectious disease when sufficient amount of population, for example 70-80% has become immune to the disease, either by contracting the disease or vaccinating thus building up the antibody towards the disease.[6]

The race towards vaccine development had actually started since the researcher found the genome of the SARS-CoV-2 (Severe acute respiratory syndrome coronavirus-2). The virus itself consisted of spike protein (S-protein), nucleocapsid, and an RNA-genome.[7] Vaccine can be generated from the substances of the virus or inactivated virus. Generally, vaccine cannot be made in a short-term study, it takes around 10-20 years to develop certain vaccine, ensuring the efficacy and effectiveness of the vaccine. Vaccine development requires prior pre-clinical and subsequent clinical stages (consisting of three phases). Clinical stage is

when the vaccine candidate is tested in human with ideal and controlled circumstances to find out the safety, efficacy, side effects, and long-term consequences of the vaccine.[8]

To date, there are more than 40 vaccine candidates in Phase I, 22 in Phase II, and 20 in Phase III.7 Moreover, two vaccines have been approved for full use, namely BioNTech-Pfizer and Moderna. Both vaccines were developed from the mRNA of the SARS-CoV-2 and reported to be available soon in Indonesia along with several other vaccines, namely Sinovac's CoronaVac, Sinopharm, and Astra Zeneca. Astra Zeneca is made using the viral vector, while Sinovac and Sinopharm are made from inactivated SARS-CoV-2.[7]

BioNTech-Pfizer, Moderna, and Astra Zeneca has included healthy, with or without comorbidities, elderly population. Both BioNTech-Pfizer and Moderna have published the Phase III result and stating that the efficacy of the vaccines was more than 94-95%[9-10], while Astra Zeneca has an efficacy of 60-90%. However, it is still the interim result of Phase III.[11]

There are three countries included in the Phase III trial of Sinovac, namely Brazil, Turkey, and Indonesia. Yet, none of the countries published the result of the phase III trial. In Brazil, the population included were all healthy adults and elderly with or without comorbidities (under-controlled). It was first reported that the efficacy was 78%, however it was later announced to be only 50.4%.[7] In Turkey, it was reported that the efficacy of Sinovac was 91.25%. How about in Indonesia? On 11th of January 2021 and 5th of February 2021, Indonesian Food and Drug Administration (FDA) gave the Emergency Use of Authorization (EUA) and declared that the efficacy was 65.3% when given to healthy adults, aged 18-59 years old without any comorbidities.[12] Side effects reported were local effects, such as fever, myalgia, and pain in the injection site. Furthermore, Phase I and II result of Sinovac vaccine in China presented that the vaccine was also safe and well tolerated to be given in healthy elderly (aged 60 years and older).[13]

Since then, The Ministry of Health (MoH) instructed that healthcare workers aged 18 years old and older should be vaccinated as soon as possible, followed by general elderly population. So, the question is, should we give the COVID-19 vaccine to the elderly? To answer that, we must remind ourselves with the physiology of aging. Aging process may decrease the immune system and response, known as immunosenescence.[14] Furthermore, aging decreases organ function and increase the risk of having comorbidities, which may hinder the effectiveness of the vaccine. Due to these circumstances, when given vaccination, elderly population may not have seroconversion rate as high as adult's population. The impact of immunosenescence was also seen in the case of Influenza vaccine which is recommended to be given annually to the adult and elderly population. A study found that although the seroconversion rate was not as high as the adult population, giving the vaccine actually protected our elderly from getting Influenza and preventing the calamitous complications, such as secondary bacterial infection that may lead to higher hospitalization rate and death.[15]

Recently, a distressing event occurred in Norway as there were at least 23 frail elderly with multiple comorbidities reported to have died following BioNTech-Pfizer vaccination.[16] Frailty is a condition where the elderly is more vulnerable to adverse health outcomes when there is an acute stressor.[17] It was narrated that they had side effects such as fever that may lead to devastating impact to their lives. It is still being investigated since then.

In Indonesia, we should take note that more than half of elderly population in Indonesia are categorized as pre-frail.[18] Only 13% of the Indonesian elderly population was categorized as robust/fit, and the rest were considered pre-frail or frail.[18] In fact, frailty is an independent risk factor for rehospitalization, dependency, and death not only due to COVID-19 but other stressors, such as side effects due to vaccination.[19]

Therefore, assessment of frailty status, for example by using FRAIL scale is a must before we give vaccination to the elderly as proposed by the Indonesian Society of Internal Medicine in concordance with the MoH. FRAIL scale as proposed by Morley, et al.[20] consisted of

five questions, including Fatigue, Resistance, Ambulation, Illness, and Loss of Weight. If the total score is more than 2, the older adult would be categorized as frail, and thus MoH of Indonesia recommended against giving the vaccine to this group of older adults. Nevertheless, not all frail elderly cannot be vaccinated as FRAIL scale is only a screening tool. Thorough consultation and frailty examination using different scale, such as Frailty Index-40 (FI-40)[21] or Clinical Frail Scale (CFS)[22] with an internist or geriatrician may be needed to establish the frail diagnosis. Perhaps, if the elderly is categorized as frail in FRAIL scale but only categorized as pre-frail by using FI-40 or mildly frail by using CFS along with the clinical judgement of the physician, he/she may still be eligible for.

Beside safety, efficacy of the COVID-19 vaccine is also an important concern as we know that frail elderly is prone to develop severe COVID-19 infection, yet the efficacy of vaccine may be decrease as shown on previous study on Influenza vaccine.[23]

Having prior vaccination or past COVID-19 does not mean that someone is totally immune to COVID-19 as a recent study suggested that the antibody related to COVID-19 past infection is significantly decreasing after 3 months post infection.[24] Compliance to implementation of health protocol remained the most crucial strategy during this pandemic.

REFERENCES

1. Komite Penanggulangan COVID-19 dan Pemulihan Ekonomi Nasional. Peta Sebaran. [cited on Jan 21 2021]. Available from: https://covid19.go.id/peta-sebaran.
2. Baxter D. Active and passive immunity, vaccine types, excipients and licensing. Occup Med (Lond). 2007;57(8):552-6. doi: 10.1093/occmed/kqm110. PMID: 18045976.
3. Riedel S. Edward Jenner and the history of smallpox and vaccination. Proc (Bayl Univ Med Cent). 2005;18(1):21-25. doi:10.1080/08998280.2005.11928028.
4. Kay AW, Blish CA. Immunogenicity and Clinical Efficacy of Influenza Vaccination in Pregnancy. Front Immunol. 2015;6:289. Published 2015 Jun 4. doi:10.3389/fimmu.2015.00289
5. Singal AG, Higgins PD, Waljee AK. A primer on effectiveness and efficacy trials. Clin Transl Gastroenterol. 2014;5(1):e45. Published 2014 Jan 2. doi:10.1038/ctg.2013.13.
6. Randolph HE, Barreiro LB. Herd Immunity: Understanding COVID-19. Immunity. 2020;52(5):737-741. doi:10.1016/j.immuni.2020.04.012
7. The New York Times. Coronavirus Vaccine Tracker. Updated Jan 19 2021. [cited on Jan 21 2021]. Available from: https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html
8. Heaton PM. The Covid-19 Vaccine-Development Multiverse. N Engl J Med. 2020;383(20):1986-90.
9. Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020;383:2603-15. DOI: 10.1056/NEJMoa2034577,
10. Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021. DOI: 10.1056/NEJMoa2035389
11. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet .2021;397:99–111.
12. The Jakarta Globe. Indonesia approves Sinovac vaccine amid dramatic surge in Coronavirus cases. [cited on Jan 21 2021]. Available from: https://jakartaglobe.id/news/indonesia-approves-sinovac-vaccine-amid-dramatic-surge-in-coronavirus-cases.
13. Wu Z, Hu Y, Xu M, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis. 2021.
14. Aw D, Silva AB, Palmer DB. Immunosenescence: emerging challenges for an ageing population. Immunology. 2007;120(4):435-446. doi:10.1111/j.1365-2567.2007.02555.x
15. Nursyirwan SA, Koesno S, Wahyudi ER, Mansjoer A. Predictor factors affecting seroconversion post-influenza vaccination in the elderly. JPDI. 2017;4(4):204-208.
16. CNN. Norway reviewing deaths of frail and elderly patients vaccinated against Covid-19. [cited on Jan 21 2021]. Available from: https://edition.cnn.com/2021/01/18/health/covid-vaccine-pfizer-deaths-norway-intl/index.html.
17. Xue QL. The frailty syndrome: definition and natural history. Clin Geriatr Med. 2011;27(1):1-15. doi:10.1016/j.cger.2010.08.009.
18. Setiati, S., Laksmi, P.W., Aryana, I. et al. Frailty state among Indonesian elderly: prevalence, associated factors, and frailty state transition. BMC Geriatr 19, 182 (2019). https://doi.org/10.1186/s12877-019-1198-8.
19. Hewitt J, Carter B, Vilches-Moraga A, et al. The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study. Lancet Public Health. 2020;5:e444–51.

20. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging. 2012;16(7):601-608. doi:10.1007/s12603-012-0084-2.
21. Searle SD, Mitnitski A, Gahbauer EA, et al. A standard procedure for creating a frailty index. BMC Geriatr. 2008;8(24). https://doi.org/10.1186/1471-2318-8-24.
22. Mendiratta P, Latif R. Clinical Frailty Scale. [Updated 2021 Feb 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559009/.
23. Andrew MK, Shinde V, Ye L, et al. The importance of frailty in the assessment of trivalent inactivated influenza vaccine effectiveness against influenza-related hospitalization in elderly people. J Infect Dis. 2017;216(4):405–14.
24. Seow J, Graham C, Merrick B, et al. Longitudinal observation and decline of neutralizing antibody responses in the three months following SARS-CoV-2 infection in humans. Nat Microbiol. 2020;5: 1598–607. https://doi.org/10.1038/s41564-020-00813-8.