

COVID-19: Herd immunity and convalescent plasma transfer therapy

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1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2, has spread worldwide triggering a pandemic. Its first case was reported in Wuhan, the capital of China's Hubei province, and since then it has spread across the world becoming one of the worst pandemics in the history of mankind.¹ Its basic reproductive number (R_0) has been determined to be 2 to 3.² Here, the basic R_0 is the average number of secondary cases generated by infected subjects in the completely susceptible population. Any pandemic with a basic R_0 less than 1 will die out on its own.³ To give a perspective to this number, the 1918 influenza pandemic which infected one-third of world's population and resulted in 50 million casualties had an R_0 of 1.8.⁴ Majority of patients with COVID-19 show mild symptoms and recover on their own in 2 to 3 weeks, so it is likely that cases could go undetected and the actual basic R_0 is much higher than stated above. COVID-19 symptoms include fever, cough, sore throat, diarrhea, shortness of breath, loss of smell/taste, and pneumonia, and in severe cases, it can lead to multiple organ failure and death.⁵ The overall rate of mortality per confirmed cases has been reported to be nearly 4.5%.⁶ The rate of recovery and severity of the disease depends on the age and health of the subjects. The younger age group without any prehealth condition is expected to have a low death rate (0.2%), whereas the older population (above 80) have much higher death rate (15%).⁶ Research is being carried out for validating the available potential treatment regime and vaccines, and for developing a new one.

2 | HERD IMMUNITY AND PLAUSIBLE STRATEGY AGAINST COVID-19

Herd immunity is an age-old concept. It is indirect protection conferred by immune individuals to the susceptible ones in a given

population against a specific pathogenic infestation. Herd immunity protects by limiting the spread of the disease.⁷ R_0 number determines the minimum percentage (Y) of the population required to be immune to achieve the herd immunity for the entire population.⁷ Here

$$Y = (R_0 - 1)/R_0 \times 100^7.$$

As described before, $R_0 = 2-3$ as per recent reports.

If $R_0 = 2$, then $Y = [(2 - 1)/2] \times 100 = 50\%$.

Similarly, when $R_0 = 3$, then $Y = [(3 - 1)/3] \times 100 = 66.66\%$

Therefore, for $R_0 = 2-3$, nearly 50% to 66.66%* (threshold) of the population is required to be immune against COVID-19 for the protection of susceptible individuals in a given population through herd immunity.

*As discussed previously, it can be higher as cases are most likely underreported.

In emergency situations, recovered subjects who are negative for COVID-19 can be considered for voluntary temporary employment at sensitive locations such as hospitals and airports as per their capability and skill set. Such locations have the potential to become the hotbed for the spread of infections. In the presence of immune volunteer workers, the spread of the disease would be restricted. The recovered individuals if placed in high enough numbers at a sensitive location can act as a source of indirect immunity⁷ and protect the target population. The coronavirus cannot reinfect the recovered subjects. Though few reports from Japan suggest the possibility of reinfection, it has been disputed by some experts who believed that redetection was due to the error in diagnosis and not the reinfection.⁸ Some health officials also considered it to be the cases of reactivation of latent COVID-19.⁸ In China, nearly 14% of patients checked for 14 days after resolution of all symptoms, showed the positive RNA test.⁹ The possibility of a mutation and emergence of a new strain of a virus cannot be ruled out and it can make herd immunity ineffective.⁷ On a positive note, induction of herd immunity by vaccination is a tried and tested

approach. All places are not equally prone to the spread of infection, especially in developing countries. Localized herd immunity can help in further impeding the spread of COVID-19.

3 | CONVALESCENT PLASMA COLLECTION

One of the investigational treatments being researched is the administration of convalescent plasma collected from recovered patients to patients with COVID-19. Here, convalescent plasma from recovered patients (or survivors) contains neutralizing antibodies against COVID-19. Most effective convalescent plasma with high titer of neutralizing antibodies as determined by enzyme-linked immunosorbent assays (ELISA) should be stored in blood banks. Previously, it has been shown that convalescent plasma transfer from recovered patients to critical subjects helped in recovering from dreadful infections such as Ebola and Influenza.¹⁰ In China, Shen et al¹¹ and Duan et al¹² have shown that convalescent plasma therapy could help in the prognosis of severe cases of COVID-19, and large-scale clinical trials are being conducted to validate their findings at several locations in the United States and Europe.¹³ The clinical trials conducted by Shen et al and Duan et al were convincing but the administration of convalescent plasma was not done in a randomized clinical trial manner and it is necessary to revalidate their findings.¹⁴ Still considering the success history of plasma therapy against Ebola and Influenza, and recovery reports from China, it looks very promising.¹⁵ The arrangement for coordination between blood centers and hospitals should be preplanned in countries where COVID-19 has just started making its mark. As per United States-Food and Drug Administration (US-FDA) guidelines,¹⁶ clinically asymptomatic survivors who have been tested negative twice should be considered for potential convalescent plasma donation. The survivor should not display any symptoms for at least 28 days after discharge or for at least 14 days after discharge and should be negative results for COVID-19 as determined by nasopharyngeal swab specimen or molecular diagnostic tests like real-time polymerase chain reaction or antibody-based assays. The records of recovered subjects should be stringently checked before considering them for potential donation. In the case of Ebola, studies have shown that not all Ebola surviving donor's convalescent plasma had Ebola neutralizing antibodies as determined by ELISA test.¹⁷ Importantly, antibody titer should be checked for each of the donated convalescent plasma. Detailed guidelines given by US-FDA¹⁶ over the inclusion and exclusion criteria for the selection of recovered patients should be considered for collection procedures and for convalescent plasma therapy.¹⁶ Also, the optimal dosage of convalescent plasma, time line of administration, and overall efficacy need more validation by larger randomized clinical trials.

4 | DISCUSSION

Physical distancing, quarantine, and other sanitizing habits have shown some success in slowing down the pandemic but it is still far

from being contained in most countries. The antimalarial drug chloroquine and antibiotic azithromycin have shown potential against COVID-19 but its efficacy has been recently disputed.¹⁸ Other potential therapeutic agents tried so far include ritonavir, favipiravir, remdesivir, ribavirin, sarilumab, and tocilumab, but their use also needs more evidence.¹⁹ Considering the plight of undeveloped and developing countries where most people cannot afford ventilators or lockdown for an extended period of time, pandemic must be slowed down so that health infrastructure can handle it efficiently. In the absence of validated treatment and tested vaccines, localized herd immunity can help us in slowing down its spread at sensitive locations. Here, convalescent plasma transfer could be the most critical weapon in the fight with COVID-19 in severe cases. Here, survivors have a key role to play in both herd immunity as well as plasma transfer. To tap the potential, all survivors should be well-documented. Their convalescent plasma should be checked for neutralizing antibodies and stored in blood banks and spread up across countries so that it can be delivered when the need arises. From the ethical point of view, there is a roadblock for taking help from survivors to this extent, but considering the necessity to safeguard the health of an immunocompromised and older population, it should be considered and steps must be taken to explain its importance to the survivors.

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How to cite this article: Syal K. COVID-19: Herd immunity and convalescent plasma transfer therapy. *J Med Virol*. 2020; 92:1380-1382. <https://doi.org/10.1002/jmv.25870>