***Convalescent plasma, Political Narrative, and Public Health Ethics in the COVID-19 Pandemic***

1) Simran Agrawal- Medical Student, Topiwala National Medical College and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India. (+918451070089, [agrawalsimran2803@gmail.com](mailto:agrawalsimran2803@gmail.com) )

2) Dr. Anup Agarwal- Public Health Practitioner, People’s Association for Equity and Health, Ambikapur, Surguja, Chhattisgarh, India. (+918582932607, [mailanupagarwal@gmail.com](mailto:mailanupagarwal@gmail.com) )

3) Dr. Yogesh Jain (Corresponding Author)- Public Health Practitioner, People’s Association for Equity and Health, Ambikapur, Surguja, Chhattisgarh, India. (+919425530357, [yogeshjain.chhattisgarh@gmail.com](mailto:yogeshjain.chhattisgarh@gmail.com) )

**ABSTRACT**

Convalescent plasma therapy emerged as an experimental therapy for the treatment of COVID-19. However, despite limited data regarding its safety and efficacy, the therapy was extensively publicized by multiple politicians as a cure. We analyze the impact of this political narrative around medical therapeutics on the pandemic using the coherentist model of Public Health Ethics. The clinical benefits of the therapy are evaluated in terms of reduction in mortality and disease progression as compared to the potential transfusion-related adverse events. Political advocacy of therapeutics might hamper the autonomy and decision-making of individuals and institutions. Marketing and monetization of convalescent plasma might cause inequitable distribution and unregulated use. It also creates an economic burden on the government and healthcare which should be justified by the additional cost/effectiveness ratio of the therapy. This article exemplifies the inadvertent effects and ethical challenges following political narratives about medical therapeutics and the importance of imbibing ethics into designing policies concerning public healthcare.

On the evening of May 15, 2020, I (SA) enrolled the first 2 patients GJ and PR at our institution in the PLACID trial, a randomized controlled trial on the efficacy of Convalescent Plasma (CP) in COVID-19(1). They were randomized into the treatment and control arm respectively. At 1 AM in a ward full of patients fighting for each breath and the monitors making a cacophony, I put my hopes in the bag of CP to fight the deadly virus. While GJ’s condition did not improve, to our surprise PR who had not received the new treatment, recovered. We subsequently enrolled 27 patients at our institution, 14 of whom received the plasma. However, there was no obvious evidence to suggest that the therapy had in any way improved the clinical outcome. Moreover, on completion of the enrollment of 464 patients across the 39 trial sites, there was no benefit of CP in the reduction of mortality or disease progression from moderate to severe disease.

While the trial was still in its early phase in May, helping us convert clinical equipoise into tangible data, a narrative rooted in populism and appeasement was being promulgated by politicians in the popular media based on anecdotal evidence about the ability of CP to fight COVID-19(2). Such publicity of medical therapeutics by political leaders may allow for early authorization and expedition of life-saving drugs but can also create unforeseen challenges; rendering such statements by political leaders a dilemma for the health professionals that should be analyzed through the lens of public health ethics.

We hereby refer to the coherentist model of public health ethics to analyze this ethical dilemma(3). It describes a methodological approach to the ethical practice of public health and provides 5 normative criteria which are 1) expected benefit 2) expected harm 3) impact on public autonomy 4) impact on equity 5) expected efficiency. We have added the impact on informed consent along with autonomy in relevance with the CP therapy.

**EXPECTED BENEFIT OF CONVALESCENT PLASMA**

The benefit of the CP can be measured in terms of reduced mortality, prevention of disease progression, negative conversion to SARS-CoV-2 viral RNA, decreased duration of hospital stay, and symptomatic relief. A randomized clinical trial with 103 patients conducted in China presented an increased negative conversion rate of the COVID-19 RT-PCR but there was no mortality benefit of CP(4). Similar results were reported by the PLACID trial in terms of mortality and negative viral RNA conversion. Additionally, on day 7 patients reported more relief in the shortness of breath and fatigue with CP(1).

**POTENTIAL HARM OF CONVALESCENT PLASMA**

Although it was historically considered a safe modality, CP transfusion can cause adverse events ranging from a mild rash to life-threatening lung injuries like Transfusion Related Acute Lung Injury (TRALI) and Transfusion Associated Circulatory Overload (TACO)(5). COVID-19 causes various pulmonary pathologies including thrombosis, embolism, and pneumonia. This pulmonary thrombosis may be worsened by the pro-thrombotic effects of plasma. Moreover, it is difficult to distinguish TRALI and TACO from the worsening pulmonary pathology due to COVID-19 and may lead to under-reporting of adverse events associated with CP(6).

These political statements on medical therapeutics and subsequent emergency authorizations are probably the results of a compelling “need to act” in a public health emergency(7). Nonetheless, they may impede the larger interest of public health by compromising the ability to recruit participants in clinical trials essential to determine the safety and efficacy of the therapy(8). While screening patients for the PLACID trial, we observed that patients would routinely opt for the off-label plasma therapy but were reluctant to consent for enrollment in the clinical trial as they may not get the desired treatment.

**IMPACT ON INFORMED CONSENT AND AUTONOMY**

The information shared by various leaders on news and social media, highlighting only the expected advantages of CP may influence the opinion of the population in a biased way obstructing their ability to make a well-informed, voluntary decision(9).

While the effect on individual patients is obvious, a more insidious effect is on the policymakers. CP made its way into the clinical management protocol of COVID-19 by the Ministry of Health, Government of India as early as mid-June(10) and was authorized for emergency use by the US-FDA in August(11). Furthermore, the advisory remains unaltered even after 2 months of publication of trial data(12). While the Indian Council of Medical Research has put out a revised advisory, it is unlikely to check the unscrupulous use of CP(13).

**MARKETING AND MONETISATION - DISPARITY IN ACCESSIBILITY AND EQUITY**

The financial burden of CP therapy should be considered for ensuring equity in distribution. There was a sudden upsurge in the demand for CP due to the hype. This facilitated a flourishing black market for the sale of CP in India. Stories of patient families spending exorbitant amounts to buy CP from potential donors were reported(14). Despite the laws against monetary compensation for blood and blood products, there were reports of compensation for plasma donation from both the private and public sectors in India(15).

**COST-EFFECTIVENESS ANALYSIS**

In a resource-limited setting, it is imperative to allocate funds after analyzing the effectiveness of the modality in comparison to other preventive and curative interventions. The process of plasma collection using apheresis, antibody testing, storage, and transfusion of CP is time-consuming, expensive, and requires a special setting and machinery(16). The pandemic has created a heavy burden on the healthcare system in the form of a shortage of hospital beds, human resources, and healthcare facilities for patients with and without COVID-19. There is an increased demand for the essential protective equipment for healthcare workers, sanitation, and infection control amenities along with the other overheads of the pandemic. Thus, it is crucial to use the resources and services cautiously in a well-planned manner(17)(18).

Marckmann et al.(3) also describe the conditions for fair decision-making in public health. This includes transparency, consistency, justification, participation, managing conflict of interest, openness for revision, and regulation. Announcements made during election campaigns, political speeches may not be conducive to a fair decision-making process as outlined above and thus overlook public health ethics.

This is just one example of political influence on the use of CP from India during this pandemic. This is not unique. There have been similar narratives creating public health dilemmas around Hydroxychloroquine and now COVID-19 vaccine(19) not only in India and the USA but in many other countries.

Political leaders design policies and guide their governance when put into practice. In the setting of a pandemic, these roles demanded that they take the help of experts in health, finance, governance, implementation, and other allied departments. In democracies, they are elected by the people and thus have an additional role of informing the people at large and engaging with them for decentralized decision making. We make a case for including principles of public health ethics in their decision making and dialogue with the community.

This also places the onus on our institutions guided by public health professionals, healthcare professionals, bureaucrats, and other policymakers to design systems, policies, and protocols rooted in ethics and not political influence.

**CONTRIBUTORSHIP STATEMENT**

The first two authors Agrawal S. and Agarwal A. were involved in planning, drafting, and editing the article. The third author Jain Y. was involved in reviewing and guidance.

**ACKNOWLEDGEMENTS**

NONE.

**FUNDING**

NONE.

**COMPETING INTERESTS**

NONE.

**ETHICAL APPROVAL**

NOT REQUIRED

**REFERENCES**

1. Agarwal A, Mukherjee A, Kumar G, Chatterjee P, Bhatnagar T, Malhotra P. Convalescent plasma in the management of moderate covid-19 in adults in India: open-label phase II multicentre randomized controlled trial (PLACID Trial). BMJ [Internet]. 2020 Oct 22;371:m3939. Available from:<http://www.bmj.com/content/371/bmj.m3939.abstract>

2. Edition E, Homes AJ. COVID-19 : Won’t stop clinical trials of plasma therapy as initial results are good, says Arvind Kejriwal. 2020; Available from <https://economictimes.indiatimes.com/news/politics-and-nation/covid-19-wont-stop-clinical-trials-of-plasma-therapy-as-initial-results-are-good-says-arvind-kejriwal/articleshow/75487345.cms>

3. Marckmann G, Schmidt H, Sofaer N, Strech D. Putting public health ethics into practice: A systematic framework. *Front Public Heal*. 2015;3(FEB):1-8. Available from: [doi:10.3389/fpubh.2015.00023](https://www.frontiersin.org/articles/10.3389/fpubh.2015.00023/full)

4. Li L, Zhang W, Hu Y, Tong X, Zheng S, Yang J, et al. Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19: A Randomized Clinical Trial. JAMA [Internet]. 2020 Aug 4;324(5):460–70. Available from:<https://doi.org/10.1001/jama.2020.10044>

5. Casadevall A, Pirofski LA. The convalescent sera option for containing COVID-19. J Clin Invest. 2020;130(4):1545–8.

6. Pathak, E. B. (2020). Convalescent plasma is ineffective for covid-19. *BMJ*, *371*, m4072. <https://doi.org/10.1136/bmj.m4072>

7. Angus DC. Optimizing the Trade-off between Learning and Doing in a Pandemic. JAMA - J Am Med Assoc. 2020;323(19):1895–6.

8. <https://www.nytimes.com/2020/08/04/health/trump-plasma.html?searchResultPosition=3>

9. Aquino YSJ, Cabrera N. Hydroxychloroquine and COVID-19: Critiquing the impact of disease public profile on policy and clinical decision-making. J Med Ethics. 2020;(1):574–8.

10. India G of M of H and FW. Clinical Management Protocol: COVID-19, MHFW, GoI. 2020; Available from<https://www.mohfw.gov.in/pdf/ClinicalManagementProtocolforCOVID19.pdf>

11. ZACHARY BRENNAN and SARAH OWERMOHLE. (2020). *The Food and Drug Administration issued an emergency authorization for blood plasma as a coronavirus treatment, the agency and President Donald*. 1–9. <https://www.politico.com/news/2020/08/23/plasma-treatment-coronavirus-fda-trump-400390>

12. Title Page Convalescent plasma in the management of moderate COVID-19 in India : An open-label parallel-arm phase II multicentre randomized controlled trial ( PLACID Trial ) Anup Agarwal, Aparna Mukherjee, Gunjan Kumar, Pranab Chatterjee, Tarun Bhatnagar. 2020;(4911):1–41.

13. Evidence Based Advisory to address Inappropriate Use of Convalescent Plasma in COVID-19 Patients. Available from: <https://www.icmr.gov.in/ctechdocad.html>

14. Tv L. Exclusive : Coronavirus pandemic fuels black-market for the plasma of recovered. 2020; Available from<https://www.indiatoday.in/india/story/exclusive-coronavirus-pandemic-fuels-black-market-for-plasma-of-recovered-patients-1703332-2020-07-22>

15. Yet NOT. Wooing Plasma Donors. 2020; Available from<https://www.indialegallive.com/special-story/wooing-plasma-donors/>

16. Epstein J, Smid WM, Wendel S, Somuah D, Burnouf T. Use of COVID-19 convalescent plasma in low- and middle-income countries: a call for ethical principles and the assurance of quality and safety. Vox Sang. 2020;1–2.

17. Gostin LO, Friedman EA, Wetter SA. Responding to Covid-19: How to Navigate a Public Health Emergency Legally and Ethically. Hastings Cent Rep. 2020;50(2):8–12.

18. Emanuel EJ, Persad G, Upshur R, Thome B, Parker M, Glickman A, et al. Fair Allocation of Scarce Medical Resources in the Time of Covid-19. N Engl J Med [Internet]. 2020 Mar 23;382(21):2049–55. Available from:<https://doi.org/10.1056/NEJMsb2005114>

19. *Coronavirus | All Indians to get free COVID-19 vaccine, says Union Minister*. (2020). 18–20. [https://www.thehindu.com/news/national/coronavirus-all-indians-to-get-free-covid-19-vaccine-says-union-minister/article32940902.ece#](https://www.thehindu.com/news/national/coronavirus-all-indians-to-get-free-covid-19-vaccine-says-union-minister/article32940902.ece)