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NEWS / HEALTH

Studies show plasma does not help COVID-19 patients but doctors still prescribe it

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A bag containing blood plasma from a donor at ILBS hospital, in Vasant Kunj, Delhi on 18 July 2020.
BIPLOV BHUYAN / HINDUSTAN TIMES

COVID-19



(/covid-19)

In November, Nitin Niranjana spent a week searching for a plasma donor for his 63-year-old mother. She was in an intensive care unit in a hospital in Delhi, hooked to a ventilator. Her health was deteriorating quickly. The hospital had a plasma bank with units that matched her blood type, but refused to give it to her till her family found a donor to replace the units of plasma the patient would use. Niranjana created a Twitter account for the first time and used it to look for donors. He even considered paying for a radio advertisement. On the sixth day of his search he found a family friend ready to donate. Niranjana is a 37-year-old government school teacher in Jalaun district in Uttar Pradesh and the

sole earning member of his family. He spent most of his life's savings for his mother's treatment. She died despite getting a plasma transfusion.

In August, *The Caravan* reported (<https://caravanmagazine.in/health/lack-of-oversight-leaves-covid-19-patients-scrambling-for-plasma>) on how COVID-19 patients and their families were scrambling for plasma. More and more doctors were recommending the treatment for which there was little regulation. In October and November, two teams of researchers from India and Argentina published separate scientific studies, both which showed that convalescent plasma therapy did not help COVID-19 patients. Even in December, people are still struggling to get plasma for severely-ill family members.

Doctors around the world have relied on experimental therapies and repurposed drugs during the coronavirus pandemic. In most cases, there was little evidence that these therapies actually worked but doctors used them as long as they believed they would do no harm. They were throwing everything at the disease, hoping something would flush the virus out of their patient's collapsing bodies. As the year progressed, medical researchers worked out which treatments work (<https://jamanetwork.com/journals/jama/fullarticle/2770279>) and which do not (<https://www.nejm.org/doi/10.1056/NEJMoa2023184>).

Plasma therapy is a process in which doctors draw blood plasma from people who have recovered from COVID-19 and transfused it into people still ill with the disease. The theory is that neutralising antibodies in plasma will help the person receiving the transfusion fight off infection. However, two randomised controlled trials indicate that plasma therapy does not decrease mortality or recovery period among hospitalised patients.

Researchers from several institutions in India conducted the PLACID study (<https://www.bmj.com/content/371/bmj.m3939>) between April and July across 39 sites and enrolled 464 hospitalised adults. The study

concluded that plasma therapy did not reduce mortality or progression towards severe disease. The second study (<https://www.nejm.org/doi/full/10.1056/NEJMoa2031304>), which researchers in Argentina carried out between May and August, enrolled 333 hospitalised patients with severe COVID-19 pneumonia, of whom 228 received plasma while others received a placebo. This study also showed that there were no significant differences in the clinical status or overall mortality between the two groups. “Both these studies are of high quality, use a large pool of patients, contain control groups and have specific endpoints that they investigate,” Dr SP Kalantri, the medical superintendent at the Kasturba Gandhi Hospital in Sevagram in Maharashtra, said. Kalantri was not associated with either study.

The one point of contention about the PLACID trial is that it did not measure the level of neutralising antibodies in the plasma given to subjects. I spoke to Pankaj Malhotra, a doctor and researcher at the Post Graduate Institute of Medical Education and Research in Chandigarh who worked on the PLACID trial. “At the time we didn’t have the resources to test all the blood plasma for the level of antibodies,” Malhotra said. “So, it does leave us with the question whether having a high level of neutralising antibodies might have made plasma therapy more effective.” He was also involved in framing the plasma therapy treatment guidelines for COVID-19. These guidelines advised against indiscriminate use of plasma and claimed that the clinical benefits depended on the concentration of specific antibodies in convalescent plasma.

Kalantri said the lack of data on antibody levels in the PLACID trial did not negate its findings. “If there is a lack of information here, this needs to be addressed using evidence based research and a well-constructed clinical trial, not with assumptions.”

An editorial in the *British Medical Journal*, a leading global publication of medical research, elaborating on the PLACID trial results laid out the

potential harm of plasma therapy. “Despite the presence in plasma of anticoagulation factors such as antithrombin and protein C, the net effect of plasma is prothrombotic,” the editorial said. This means that transfused plasma can potentially promote formation of blood clots, despite having components that act as anticoagulants or blood thinners. This is an added risk for COVID-19 patients since the disease already causes clotting and related life-threatening complications.

Overall, scientific studies lean heavily towards the conclusion that plasma therapy is ineffective against COVID-19. “On convalescent plasma therapy, there is no ambiguity left now,” Amar Jesani, editor of the *Indian Journal of Medical Ethics*, a journal for research and discussion on ethics and humanities related to healthcare, said. “The medical practitioners not heeding the science are doing a disservice to their patients.”

But these studies have made no dent in the demand for plasma in India. Doctors have continued to prescribe plasma therapy. Like Niranjana, frantic family members of COVID-19 patients’ have flooded social media with messages asking for plasma. “People don’t care about scientific evidence,” a doctor running a government funded plasma bank in Delhi who asked not to be identified, said. “And even doctors have faith in the therapy.”

Most doctors I spoke to in November said they continued to prescribe plasma therapy for COVID-19 because they observed their patients recover. “I have seen that if prescribed to patients in combination with steroids and anticoagulants, at the time when patients’ oxygen is dropping or they are getting sicker, it does help,” Dr S Chatterjee, internal medicine specialist at the Indraprastha Apollo Hospital in Delhi, said. Meanwhile, Malhotra recognised the significance of the new evidence but was not ready to rule plasma therapy out. “I am not saying we should prescribe it indiscriminately, but I have observed that it can be

useful in patients just when they are at the cusp of turning seriously ill,” he said.

The story of plasma therapy during the 2020 pandemic is about how doctors make decisions between quickly evolving scientific understanding and what they believe they observe first-hand. Dr Sahaj Rathi, an internal medicine faculty at the Mahatma Gandhi Institute of Medical Sciences, said he understood why doctors relied on plasma therapy in the early days of COVID-19. “I believe this comes out of a desire to help. However, this is not how evidence based medicine works,” he said. “With two trials showing plasma works neither in mild nor in severe disease, and no trials which show it does, it is high time we stop using it in clinical practice.” Rathi and Kalantri wrote (<https://ijme.in/articles/ethics-of-clinical-research-and-practice-in-india-during-the-covid-19-pandemic/?galley=html>) a critique of experimental COVID-19 therapies in the *Indian Journal of Medical Ethics* in which they explain why doctors should not prescribe medicines of uncertain efficacy simply because they lack treatment options. A summary in the *Lancet*, one of the best known peer-reviewed medical journals, in 2017 laid out the rationale for relying on data from well-designed trials over anecdotes or incidental observation: “Controlled clinical observations provide more trustworthy evidence than do uncontrolled observations, biological experiments, or individual clinician's experiences.”

Much of plasma therapy's popularity is due to Arvind Kejriwal, the chief minister of Delhi, and other politicians who promoted it uncritically. One news report even claimed (<https://theprint.in/health/how-amit-shah-has-given-plasma-therapy-a-new-lease-of-life-after-icmr-junked-it/545817/>) that the ICMR wanted to remove plasma therapy from COVID-19 treatment protocol but kept it at the request of home minister Amit Shah. “It is hard for government officials and our politicians to admit they were wrong, when they have already injected people with false hope for a so-called cure,” Kalantri said.

With overwhelming evidence against the efficacy of plasma therapy and apprehensions regarding its safety, why are distressed family members left to struggle to find plasma? “Why is our government letting this happen?” Rajat Agarwal, a blood donation coordinator at Sankalp India Foundation, a non-profit in Bangalore, asked. “There are no stringent regulations in place, nor does any relevant government authority care to look into what our patients are subjected to.”

Niranjan’s mother died on 29 November. He still thought it might have been because it took him six days to find a plasma donor. “I pleaded with the doctors to give her the plasma until I arrange a donor, but they did not budge,” he said. “I wonder if I had been quicker to source the plasma, it would have made a difference.”

Niranjan had lost faith in the healthcare system. “I don’t know whether to believe these hospitals have our best interests at heart, or they are here just to fleece us,” he said. “Be it plasma therapy or anything else, at the time I had no option but to do whatever they asked me to do, because I didn’t know how else to save my mother.”

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