

NO CORRELATION BETWEEN CT VALUES AND COVID-19 SEVERITY

Relevant for: Developmental Issues | Topic: Health & Sanitation and related issues

Inaccurate indicator: The RT-PCR test presently being conducted is qualitative in nature and may only give a rough estimate of viral load.

Currently in India, RT-PCR tests can tell if a person is infected with novel coronavirus or not. It does not reveal the amount of virus (viral load in scientific parlance) present in the person. But there is an indirect way of knowing the amount of virus that a person might be harbouring.

The PCR test amplifies the genetic material from coronavirus through multiple cycles. Since coronavirus has RNA, it is first converted into DNA, and each cycle of amplification doubles the amount of DNA. If there is just one DNA molecule to start with, the amount of DNA after 30 cycles of amplification will be 2³⁰ (2 raised to 30) times, or one billion molecules. If there is more genetic material to begin with, then fewer cycles of amplification would be sufficient to detect the DNA.

Writing in her blog, Dr. Kiran Mazumdar-Shaw of Biocon says that when she got her sample tested for coronavirus infection with RT-PCR, she asked for the cycle threshold (Ct) value to assess her viral load. She decided to home quarantine under tele-supervision as the Ct value was 23 (meaning only 23 cycles of amplification were needed for DNA detection). She then says: "My RT-PCR test on day 10 was still positive but with a Ct value of 33, suggesting a very low and non-infectious viral load generally attributed to dead virus shedding."

While the cycle threshold value can be suggestive of the amount of virus in an infected person, there is no reliable way of correlating the Ct value with COVID-19 disease severity or infectiousness.

"There are no studies to show correlation of disease severity and Ct value. A low Ct value indicates higher viral load, and this may be correlated to a person being more able to transmit the virus (infectious). I must caution that transmission depends on many other factors, so there is no direct correlation," virologist Dr. Shahid Jameel, CEO of DBT-Wellcome Trust India Alliance says in email to *The Hindu*.

"In my view, there is a relationship between cycle threshold value and the probability of shedding infectious virus, the lower the number the higher the likelihood. But there is no real evidence-based established number where you can say, above 30 [Ct value], you will definitely not be infectious. That said, by [Ct value] 35 you will be unlikely to be infectious," Dr. Gagandeep Kang, Professor of Microbiology at CMC Vellore says in an email to *The Hindu*.

A paper published in the *European Journal of Clinical Microbiology & Infectious Diseases* says: "Patients with Ct above 33-34 are not contagious and thus can be discharged from hospital care or strict confinement for non-hospitalised patients."

In a July 27 letter to the Chief Secretary of Karnataka, Dr. Balram Bhargava, Director-General of ICMR, says that there are "no reliable studies to definitively prove a direct correlation between disease severity/infectiousness and Ct values."

Unlike measurements made using a blood sample, real-time RT-PCR is not an absolute but only

a relative measure of viral load. “RT-PCR test presently being conducted is qualitative in nature. Ct values may give only a rough estimate of viral load,” Dr Bhargava says.

The Ct values can vary depending on how the sample has been collected. Very often, a poorly collected nasopharyngeal or oropharyngeal swab can have very high Ct values, thus leading to incorrect conclusions about infectiousness or disease severity.

“Ct values are also determined by technical competence of the person performing the test, calibration of equipment and analytical skills of the interpreters,” Dr. Bhargava notes. There have been umpteen instances when people have tested positive one day and negative the next day and again tested positive another day.

The Ct values can also vary depending on the kind of specimens collected from the same person. For instance, nasopharyngeal and oropharyngeal samples collected from the same person can have different viral loads, making Ct value a less reliable measure to assess a person’s infectiousness or disease severity. Also, the amount of virus present in nasopharyngeal and oropharyngeal samples can vary when collected at different times even on a single day.

Patients in early symptomatic phase may have relatively less viral load and hence have high Ct value, which may subsequently change. “In such cases, high Ct values will give a false sense of security,” Dr. Bhargava says. “Viral loads will increase with time and then go down. It would be a sort of bell-shaped curve,” elaborates Dr. Jameel.

Besides the amount of virus present in a person, disease severity depends on host factors. “Some patients with low viral load may suffer from very severe disease due to triggering of the immunological responses. Hence high Ct values [reflecting low viral load] may give a false sense of security,” the Dr. Bhargava adds.

The high sensitivity and the nature of PCR test that looks only at the genetic material and not the virus itself can produce false positives even when the person has fully recovered as seen in over 260 people in South Korea who tested positive after recovering. But later studies found that PCR was detecting just the dead viral fragments. High Ct values may thus mean either low levels of virus or fragments of viral RNA.

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