

## What is behind COVID-19 deaths

Accumulation of coronavirus in the lungs is the most likely cause of high mortality rates due to the COVID-19 pandemic according to a new study. These findings contradict earlier opinions that simultaneous infections such as bacterial pneumonia or overreactions of the immunological defence system of the body, played important roles in the increased risk of mortality. As of 10 October 2021, there have been 238.37 million confirmed cases of COVID-19 and 4.86 million fatalities globally. Experts link the significant mortality seen in previous viral pandemics, such as the 1918 Spanish flu and the 2009 swine flu, to a secondary bacterial infection. However, it was unclear if individuals with COVID-19 experienced a similar issue.

The latest study, led by experts from New York University (NYU) Grossman School of Medicine, USA, found that those who died due to COVID-19 had ten times the amount of virus, or viral load, in their lower airways than extremely sick patients who survived the disease. They did not find evidence linking the mortalities to a subsequent bacterial infection, probably due to the repeated course of antibiotics given to severely ill patients. The above findings show that the body's inability to deal with the large number of viruses invading the lungs is the main cause for COVID-19 fatalities.

The researchers obtained bacterial and fungal samples from the lungs of 589 people admitted to NYU Langone facilities in Manhattan and Long Island, all of whom needed mechanical ventilation. They assessed the quantity of the virus in the lower airways of 142 patients who also had a bronchoscopy surgery to clean their air passages, and identified the bacteria present by examining tiny fragments of the genetic code of the germs. They also examined the different types of immune cells and chemicals found in the lower airways. Among the observations was that those who died had on an average 50% reduced production of a certain type of immune chemical that targets the viral disease compared to COVID-19 patients who survived it. These modified proteins are part of the adaptive immune system of the body, which is a group of cells and molecules that 'remember' freshly encountered

invading microorganisms, making the body better equipped for future exposure. The researchers emphasized that they only studied coronavirus patients who had survived the first two weeks of hospitalization, and it is possible that bacterial infections or autoimmune responses had a larger role in COVID-19 deaths that occurred earlier.

The Centers for Disease Control and Prevention (CDC), USA, currently does not recommend the use of antivirals such as remdesivir for critically ill patients on mechanical ventilation. However, the above findings show that these medicines may be helpful in treating such patients. According to the researchers, their study was aimed to shed light on the impact of secondary infections, viral load and immune cell types in COVID-19 mortality. The report provides the most thorough survey of the lower airway environment in coronavirus patients. Corticosteroids and remdesivir, two medicines that presumably impact the lower airway microbial landscape, were barely utilized during the initial surge, which is in contrast to current treatment methods in COVID-19 patients. The usage of these medicines, however, was not shown to be related to the clinical outcome.

It is worth noting that despite the institutions being in 'surge mode', neither the Long Island nor Manhattan campuses experienced a shortage of medical staff, resources or equipment, and the decision to begin mechanical ventilation (MV) did not deviate from the standard of care. The cross-sectional design of this study prohibited assessing the temporal dynamics of the microbial population or the host immunological response in this cohort, both of which might have offered valuable insights into the aetiology of this illness. It is worth mentioning that there were no statistically relevant variations in sample collection time between the three result groups. Monitoring of microbial signals at early stages of the illness may also be necessary to identify alterations that occur prior to the usage of broad-spectrum antimicrobials. Furthermore, results from the lower airway samples are limited to individuals who had a bronchoscopy as part of their medical treatment. As a result, the culture-

independent data are skewed toward individuals who, while severely infected with COVID-19, were not typical of the disease extremes. Studies focused on early specimen collection duration to include subjects on MV with early death or early successful cessation of MV may be needed.

In summary, a first assessment of the lower airway microbiome utilizing a metagenomic and meta-transcriptomic method, as well as host immune profiling, is provided in severely sick COVID-19 patients requiring invasive MV. The RNA metatranscriptome analysis revealed a link between SARS-CoV-2 abundance and mortality, which was similar with the signal obtained when viral load was measured by targeted real-time reverse transcription polymerase chain reaction. These viral profiles were associated with lower anti-SARS-CoV-2 spike IgG levels and host transcriptome profiles in the lower airways, both of which were associated with a terrible outcome. Notably, no indication of a link between untreated illnesses with secondary respiratory pathogens and death was observed using both culture and NGS data. These findings imply that active lower airway SARS-CoV-2 replication and inadequate SARS-CoV-2-specific antibody responses are the primary causes of higher mortality in COVID-19 patients who require MV. The possible function of oral commensals like *M. salivarium* must be studied further. *M. salivarium* may have an effect on critical immune cells, and it has recently been found to be common in patients with ventilator-acquired pneumonia. The revelation that SARS-CoV-2 evades and/or disrupts effective innate/adaptive immune responses implies that therapies aimed at controlling viral replication or inducing a tailored antiviral immune reaction may be the most viable technique for SARS-CoV-2-infected hospitalized patients who need invasive MV. The research team also plans to monitor how the microbial population and immune system in the lungs of coronavirus patients evolve over time.

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