Medical Xpress

Long COVID affecting more than half of patients six months on

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Credit: Murdoch University

Research has revealed non-hospitalized COVID-19 patients continue to present symptoms long after infection and even more have blood biochemical abnormalities.

Scientists working at the Australian National Phenome Centre (ANPC) have investigated the blood chemistry of patients three months after the

acute disease phase of COVID-19 and found persistent systematic changes that relate to ongoing symptoms at six months.

Those symptoms include chronic fatigue, muscle and joint pain and loss of sense of smell.

"This is an immensely dangerous disease that is not only costing lives today, but as we're discovering now, may have serious health consequences for some patients long into the future, even in relatively mild original cases," said ANPC Director Professor Jeremy Nicholson.

The research into post-acute COVID-19 syndrome (PACS) – colloquially known as "long COVID"—shows that more than half of non-hospitalized COVID-19 patients had between one and nine more persistent symptoms.

"As patients who suffered from less severe manifestations of COVID-19 constitute the largest proportion of the post COVID-19 population, now over 160 million cases worldwide, we are undertaking follow up studies to assess recovery and what we've found is cause for concern.

"What we discovered is a majority of non-hospitalized COVID-19 patients are not back to normal health or normal biochemistry three months on, with one or more symptoms persisting in 57% of those patients up to six months following the acute phase."

"This is a major public health concern and warrants further investigation at the national and international level," said Professor Nicholson.

"Now that we have developed an objective metabolic framework for measuring systemic recovery in COVID-19 patients, we can use this to definitively track whether people are in fact fully recovering from the disease."

Not all people recover in the same way and there is a diversity of metabolic abnormality as well as symptoms.

"Some biochemical patterns related to heart disease and atherosclerosis risk, which are enhanced in acute phase COVID-19, do appear to normalize at least in these mildly affected patients, so it is not all bad news."

It remains unclear whether PACS is an extension of the COVID-19 disease trajectory or marks the onset of additional, separate chronic disease entities that continue to be driven by the enhanced immune response to the virus.

"There is a great deal of variation in PACS phenotypes that may require new personalized treatments," said Professor Nicholson.

"Although the actual disease presentation and the clinical severity classifications are dominated by the respiratory pathology, these symptoms are just the tip of the iceberg in terms of the underlying biochemical and immunological dysfunction caused by COVID-19."

"There are now over 140 million so-called "recovered" people around the world, so it is possible that long-term effects will be seen in tens of millions of people with significantly increased healthcare economic burdens as well as the individual medical problems."

The study provides a framework to accurately identify those suffering long-term effects and what those effects are, which is critical to developing the personalized long-term treatments that they may need.

However, further studies on wider population sets are required to validate the definitive combinations of biomarkers needed for long-term monitoring.

"We have started this validation in larger scale follow-up sample collections from COVID-19 patients that we have collected from other populations, and so far this confirms our findings; this is a job in progress," said Professor Nicholson.

Professor Bu Yeap, an Endocrinologist from the University of Western Australia (UWA) who was also involved in the study, said the research marks an important milestone in delivering better care to those affected.

"The results show that there are persisting metabolic and inflammatory changes in patients after acute COVID-19 infection, which relate to some Long COVID symptoms," said Professor Yeap.

Professor Toby Richards, who heads the clinical trials team at UWA, said it was the result of a robust collaboration effort.

"This work highlights how in Western Australia, with the COVID Research Response Trial led by UWA, the ANPC, Spinnaker Health Research Foundation and South Metropolitan Health Service, we can bring together top doctors and internationally respected scientists to develop ground-breaking research for patient benefit that has both national and international reach and impacts."

Dana Henderson, CEO of the Spinnaker Health Research Foundation which funded the studies, said addressing the ongoing health issues caused by COVID-19 is crucial.

"This research clearly demonstrates this is a long-term disease for many people infected and must compel us to also take a long-term view of recovery. We cannot ignore these findings. The individual, social and economic impacts need to be carefully considered and planned for," said Ms Henderson.

The peer reviewed paper is published in the *Journal of Proteome Research*.

More information: Nathan G. Lawler et al. Systemic Perturbations in Amine and Kynurenine Metabolism Associated with Acute SARS-CoV-2 Infection and Inflammatory Cytokine Responses, *Journal of Proteome Research* (2021). DOI: 10.1021/acs.jproteome.1c00052

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