For Long COVID Routine Lab Tests Fail to Identify Reliable Biomarkers

A recent study published investigated clinical laboratory markers of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and its post-acute sequelae (PASC).

PASC, or long COVID, is a significant health burden reported in millions of individuals worldwide. It is an umbrella term for diverse symptoms and conditions that linger following SARS-CoV-2 infection. Although potential pathogenesis models, including gut dysbiosis, endothelial dysfunction, organ injury, viral persistence, and immune dysregulation, have been postulated, there are currently no validated PASC biomarkers.

The authors developed a PASC index based on 12 symptoms distinguishing previously infected people from non-infected individuals. Moreover, they also identified various PASC clusters or sub-phenotypes. Clinical laboratory tests that distinguish between individuals with and without PASC might help in PASC diagnosis, prevention, prognosis, and treatment. While studies have identified potential PASC-associated biomarkers, they reported inconsistent findings.

Besides, systematic reviews have reported candidate categories for biomarkers, such as hematologic, inflammatory, and coagulation. In addition, viral, hormonal, and autoimmune biomarkers related to PASC phenotypes have been reported. Nevertheless, many studies have been limited by shorter follow-up periods, small sample sizes, and appropriate controls.

Importantly, a PASC index of 0 does not necessarily mean the absence of symptoms or PASC but rather that individuals with this score are unlikely to have PASC.

Study

In the present study, researchers evaluated clinical laboratory biomarkers of SARS-CoV-2 infection and PASC. People aged ≥ 18, regardless of prior SARS-CoV-2 infection, were recruited in the United States (US). Subjects completed a physical examination and surveys and provided samples for laboratory tests at enrolment.

Laboratory samples were obtained at five additional time points after the index date, i.e., the date of infection (or negative test result for non-infected individuals). The study's outcome was laboratory measures six months after the index date. Exposures were SARS-CoV-2 infection history and PASC classification. Laboratory measures included 25 routinely used, standardized tests.

The previously reported PASC index was computed. PASC index ≥ 12 was deemed an optimal threshold beyond which individuals were likely to have PASC. PASC sub-phenotypes were defined

as clusters 1–4. Cluster 1 represented a high frequency of smell/taste impairments, whereas cluster 2 represented an increased frequency of fatigue and post-exertional malaise (PEM).

In cluster 3, brain fog, fatigue, and PEM were more frequent, while cluster 4 represented increased frequency of palpitations, gastrointestinal symptoms, brain fog, PEM, dizziness, and fatigue. In the primary analysis, the team assessed whether SARS-CoV-2 infection resulted in persistent abnormalities in laboratory measures between those with and without prior infection.

In the secondary analysis, infected individuals with a PASC index ≥ 12 were compared with those with a PASC index equal to zero. In sensitivity analyses, participants with an immunological condition or diabetes were excluded. Exploratory analyses compared participants with prior infection within PASC clusters to those with a PASC index equal to zero.

Results

The study enrolled 10,094 individuals; 8,746 were previously infected. Most participants were females (72%) and fully vaccinated (62%) on the index date. The PASC index was 12 or higher for 21.5% and zero for 38.3% of previously infected individuals. The mean platelet count, glycated hemoglobin (HbA1c) levels, and urinary albumin-creatinine ratio (uACR) differed between subjects with and without previous infection.

Previously infected participants had higher mean uACR and HbA1c levels but a lower mean platelet count than non-infected subjects. However, the difference in HbA1c levels was attenuated after excluding those with preexisting diabetes. In contrast, the difference in platelet count was sustained after excluding those with an immunological condition.

Despite these observed differences, the study emphasized that there were no clinically meaningful differences in laboratory measures between previously infected individuals with a PASC index ≥ 12 and those with a PASC index equal to zero. In exploratory analyses, elevated high-sensitivity C-reactive protein (hsCRP) was noted in clusters 1 and 4, and higher calcium and lower sodium levels were observed in cluster 2 relative to those with a PASC index of zero. No differences were observed in cluster 3.

Conclusion

In sum, routine clinical laboratory measures were not reliable biomarkers of prior SARS-CoV-2 infection, PASC, or its subtypes. However, while there were minor differences in some measures between previously infected and non-infected participants, these were not clinically meaningful and might have been due to chance. Thus, understanding the biological basis of symptoms post-SARS-CoV-2 infection will require rigorous efforts beyond routine laboratory tests to identify novel biomarkers.

Source:

https://www.news-medical.net/news/20240813/Routine-lab-tests-fail-to-identify-reliable-biomarkers-for-long-COVID-study-finds.aspx