In Long COVID in South Korea and Japan have Short- and Long-Term Neuropsychiatric Outcomes

Researchers used a large, binational cohort (total n = 4,731,778) to investigate the short- and long-term associations between SARS-CoV-2 infections and subsequent adverse neuropsychiatric outcomes. They used exposure-driven propensity score matching to compare their samples' outcomes against the general population and individuals with a non-SARS-CoV-2 respiratory infection.

Study findings revealed that COVID-19 survivors were at significantly heightened risk of developing cognitive deficits, insomnia, encephalitis, and at least four other neuropsychiatric sequelae. Specific conditions included Guillain-Barré syndrome (aHR, 4.63), cognitive deficit (aHR, 2.67), insomnia (aHR, 2.40), anxiety disorder (aHR, 2.23), encephalitis (aHR, 2.15), ischaemic stroke (aHR, 2.00), mood disorder (aHR, 1.93), and nerve/nerve root/plexus disorder (aHR, 1.47). Encouragingly, vaccination was observed to attenuate the neuropsychiatric effects of the infection. These results are particularly interesting to clinicians and healthcare policymakers as they imply that the early management of COVID-19 may help their patients' short- and long-term mental health.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused coronavirus disease 2019 (COVID-19) pandemic remains one of the worst disease events in recorded human history, infecting approximately 700 million individuals and claiming more than 7 million lives in the three years since its discovery. Unfortunately for its survivors, the condition has been observed to induce long-term physical and psychological ailments that persist well past the disease's primary infection.

This colloquially termed 'long-COVID' has been loosely defined as a multisystemic illness of persistent or newly developed COVID-19 symptoms or comorbidities that remains present for three or more months following recovery from the primary SARS-CoV-2 infection. Alarmingly, the number of long-COVID patients is estimated to be between 18% and 70% of COVID-19 survivors, with recorded numbers (more than 65 million confirmed patients) assumed to be but a fraction of its undocumented global prevalence. Long-COVID thus represents one of the most oppressive healthcare concerns of the modern age.

Long-COVID is a recently described and, therefore, relatively poorly understood disease. A growing body of research demonstrates the association between long-COVID and

neuropsychiatric conditions such as depression, insomnia, anxiety, and cognitive dysfunction, with durations often exceeding six months. Unfortunately, previous studies aiming to evaluate psychiatric risks in COVID-19 survivors versus the general populace suffer from small sample sizes, limited follow-up durations, and, most notably, highly biased hospital-derived cohorts. The outcomes of such studies are confounding, thereby damping Long-COVID management and mitigation efforts.

Study

The present binational (South Korea and Japan) study aims to assess the relative risk of adverse neuropsychiatric outcomes in COVID-19 survivors versus the general populace. It also compares this risk between the former cohort and survivors of another respiratory infection (ARI). For this study, primary exposure comprised the onset of laboratory-confirmed COVID-19 (or ARI), while the primary outcome consisted of diagnosing one of 13 groups of neuropsychiatric disorders.

The study dataset was divided between 'discovery' and 'validation.' The discovery dataset was obtained from the K-COV-N cohort, a population-based, nationally representative summation of the South Korean National Health Information Database (n = 10,027,506). The validation dataset was derived from the Japanese claims-based cohort (JMDC; n = 12,218,680). Both datasets included patient-level age (>20 years), sex, income, medical history, region of residence, and insurance claims data. All participant outcomes were recorded using the World Health Organization's (WHO's) International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes.

The study methodology used exposure-driven propensity score matching to establish baseline-corrected comparisons between COVID-19 survivors and the general populace or ARI. This served the dual purpose of evaluating the robustness of observations and generalizing study findings across the large binational sample cohort.

Statistical analyses included the computation of Cox proportional hazards regression models ('adjusted hazards ratios [aHR]') to estimate short-term, long-term, and overall neuropsychiatric risk between included sample subgroups (SARS-CoV-2 infection and ARI), thereby inducing reverse causation. Covariates were accounted for by including Charlson comorbidity indices, smoking status, physical activity levels, alcohol consumption, and body mass indices (BMIs) of included participants.

Results

The discovery and validation cohorts initially comprised 10,027,506 and 12,218,680 participants, respectively. Exclusion of individuals with incomplete health records, a previous history of neuropsychiatric disorders, COVID-19 and ARI coinfections, and multiple confirmed COVID-19 reinfections resulted in a final sample size of 4,731,778 participants. The mean age of study participants was found to be 48.4 years, with 50.1% of individuals being male.

Exposure-driven propensity score matching results suggested a 1:4 ratio for COVID-19 versus the general population (discovery/South Korean sample), 1:2 for COVID-19 versus the general population (validation/Japanese sample), and 1:1 across both COVID-19 versus ARI (discovery and validation) comparisons.

Short-term (<30 days following infection recovery) risk assessments revealed that COVID-19 survivors had a substantially elevated risk of neuropsychiatric events (aHR = 2.35) compared to

the general populace, with some conditions, particularly encephalitis (aHr = 12.34), Guillain-Barré syndrome (aHR = 11.89) and insomnia (aHR = 5.36) presenting alarmingly increased risk. These findings were consistent (albeit attenuated) with those observed in SARS-CoV-2 infection versus ARI comparisons, with the former presenting an aHR of 1.36 compared to the latter.

Long-term risk assessments similarly revealed that COVID-19 survivors were significantly more likely to retain neuropsychiatric disorders for longer than 30 days when compared to the general populace and ARI (aHR = 1.71 and 1.60, respectively).

"Guillain-Barré syndrome had the highest hazard ratio post-COVID-19 diagnosis (aHR, 4.63; 95% CI, 1.66–12.98), followed by cognitive deficit (aHR, 2.67; 95% CI, 1.39–5.15), insomnia (aHR, 2.40; 95% CI, 2.15–2.69), anxiety disorder (aHR, 2.23; 95% CI, 2.08–2.40), encephalitis (aHR, 2.15; 95% CI, 1.18–3.94), ischaemic stroke (aHR, 2.00; 95% CI, 1.64–2.44), mood disorder (aHR, 1.93; 95% CI, 1.77–2.09) and nerve/nerve root/ plexus disorder (aHR, 1.47; 95% CI, 1.36–1.59)."

Time attenuation evaluations revealed that while South Korean individuals returned to near general populace risk levels in 12 months following initial infection recovery, the same was not valid for the Japanese cohort. Encouragingly, the patient-level risk of neuropsychiatric events was strongly associated with infection severity and vaccination status – risks were lower in mild SARS-CoV-2 infections and when multiple vaccinations were received.

Conclusion

The present study establishes the link between COVID-19 infections and a subsequently heightened risk of neuropsychiatric sequelae development in South Korean and Japanese natives. Furthermore, it is the first to compare this risk between COVID-19 survivors, the general population, and other respiratory infections. While time attenuation results highlight Japanese individuals as having persistent risk even after 12 months of COVID-19 recovery, insights into the associations between infection severity/vaccination status and risk can better equip clinicians and healthcare policymakers to manage their patients and this silent global pandemic.

Source:

https://www.news-medical.net/news/20240627/New-study-links-COVID-19-to-lasting-neuropsychiatric-issues-highlights-vaccination-benefits.aspx