Pre-infection serum amino acids and the incidence of long COVID among healthcare workers

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Objective : To investigate the association between serum amino acids before SARS-CoV-2 infection and the incidence of long COVID.

Methods : This is a repeat serological survey among staff members at a tertiary hospital in Tokyo. A total of 2201 SARS-CoV-2-naïve individuals in June 2022 were followed for SARS-CoV-2 infections until June 2023 using data from an in-house registry and the follow-up questionnaires. Long COVID, defined as symptoms persisting ≥4 weeks after SARS-CoV-2 infection, was ascertained via a follow-up questionnaire. Baseline serum amino acids were quantified using liquid chromatography-tandem mass spectrometry. Odds ratios of long COVID per quartile increase in each amino acid level were estimated by multivariable logistic regression while adjusting for age, sex, smoking status, alcohol consumption, leisure-time physical activity, balanced diet, BMI, the number of comorbidities, and immunosuppressive medication use.

Results : Among the 551 participants detected as COVID-19 cases during the follow-up, 177 cases (32.1%) experienced any symptoms of long COVID. Higher pre-infection serum levels of hydroxyproline, citrulline, valine, tryptophan, and β-alanine were each associated with increased odds of developing long COVID. In the analysis by type of symptoms, higher serum proline and β-alanine were associated with higher odds of general symptoms (tiredness/fatigue or fever); higher serum proline, hydroxyproline, lysine, tyrosine, tryptophan, β-alanine, methionine, and asparagine were significantly associated with higher odds of neurological symptoms (e.g., anxiety/depression, sleep problems); and higher serum hydroxyproline and citrulline were associated with higher odds of respiratory and cardiac symptoms (e.g., difficulty breathing, cough).

Conclusions : Our finding suggests that pre-infection amino acid profiles are potential predictors of long COVID.

Reassessing the impact of HTLV-1 infection on all-cause mortality: The Nagasaki Islands Study

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Objective : Prior studies have reported that human T-lymphotropic virus 1 (HTLV-1) infection increases all-cause mortality; however, as these studies were conducted in the 1980s and 1990s, it is important to reassess mortality in the contemporary population.

Methods : We conducted a cohort study in an HTLV-1 endemic area of Japan to investigate the association between HTLV-1 infection and all-cause mortality in participants from an ongoing population-based cohort. A total of 4,302 residents (39.4% men; mean age, 68.1 years), mostly middle-aged and older adults, were enrolled between April 2016 and January 2023. HTLV-1 carriers were identified using chemiluminescent enzyme immunoassays followed by confirmatory testing, with a carrier prevalence of 16.0%. Data on death certificates and residential migration were obtained from municipal registries. Person-years were calculated from the date of first participation until death, moving out, or the end of follow-up (March 31, 2023), whichever came first. Hazard ratios (HRs) and 95% confidence intervals (CIs) for all-cause mortality were estimated using panel-stratified Cox proportional hazards models, with baseline periods divided into annual panels to account for potential differences in baseline hazards. Multivariable models were adjusted for age, sex, smoking, alcohol consumption, and exercise habits, in addition to age- and sex-adjusted models.

Results : During 22,725 person-years of follow-up, 243 participants died. Among HTLV-1 carriers, the age- and sex-adjusted HR (95% CI) for all-cause mortality was 1.00 (0.73–1.37), and the multivariable HR was 1.02 (0.74–1.40), compared with non-carriers.

Conclusions : HTLV-1 infection was not associated with all-cause mortality among predominantly middle-aged and older Japanese residents living in a highly endemic area.

SARS-CoV-2 cumulative infection and its associated factors among healthcare workers in Japan

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Introduction : Evidence is scarce on cumulative SARS-CoV-2 infections among healthcare workers during the pandemic. This study aimed to describe cumulative infections, including undiagnosed cases, and identify factors associated with infection in healthcare workers in Japan.

Methods : Using serosurveys conducted across six national centers in Japan, we tracked COVID-19 cumulative infections. Seropositivity was defined as a positive result for SARS-CoV-2 nucleocapsid protein using the Roche assay, and cumulative infection was defined as the proportion of participants who tested positive for anti-nucleocapsid antibodies and/or self-reported a history of laboratory-confirmed or clinically diagnosed COVID-19 since the start of the pandemic. A Poisson regression model was performed for factor analysis using data from September 2023.

Results : Cumulative infection, which was less than 5% till the end of 2021, has increased after the emergence of the Omicron variant. Specifically, cumulative infection reached 14.6% in July 2022 (BA.1/2), 37.4% in December 2022 (BA.5), 53.3% in September 2023 (XBB subvariants), and 71.5% in December 2023 (JN.1 subvariant). The proportion of undiagnosed infections decreased from 60.9% in December 2020 to 24.7% in December 2023. Individuals aged 60 years or older had a significantly lower cumulative infection than those aged under 30 years (prevalence ratio: 0.67; 95% confidence interval: 0.59–0.77). Physicians and nurses had significantly higher cumulative infections than administrative staff, with prevalence ratios of 1.09 (95% confidence interval: 1.01–1.18) and 1.18 (95% confidence interval: 1.08–1.30), respectively.

Conclusion : Among healthcare workers in Japan, cumulative SARS-CoV-2 infection markedly increased after the emergence of the Omicron variant, whereas the proportion of undiagnosed infections has decreased throughout the pandemic. Younger people, as well as physicians and nurses, have faced a higher risk of infection.

Incidence of COVID-19 Hospitalization and Seizure by Vaccination in Youth in Japan: VENUS Study

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Background : The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Omicron variant has been reported to cause seizures more frequently and is associated with a higher risk of neurological complications in children compared to earlier variants. This study aimed to assess the incidence rates of Coronavirus Disease 2019 (COVID-19)–associated hospitalizations and seizures among children and adolescents by COVID-19 vaccination status and to compare incidence rate ratios (IRRs) between vaccinated and unvaccinated groups.

Methods : We conducted a retrospective cohort study using a database linking health insurance claims and vaccination records from seven municipalities in Japan. Individuals aged 6 months to <18 years were followed from January 1, 2022, to March 31, 2023, when the Omicron variant was predominant. Crude incidence rates of hospitalizations and seizure were calculated by vaccination status: unvaccinated versus fully vaccinated (≥2 doses, ≥14 days after the second dose). IRRs were estimated using Poisson regression models, adjusting for age group, sex, municipality, and the presence of chronic medical conditions.

Results : A total of 72,343 individuals were included; 51.5% were male, and 7.0% had at least one chronic medical condition. There were 75 hospitalizations and 131 seizure. Crude incidence rates of hospitalizations were 8.3 per 100,000 person-months (95% confidence interval [CI]: 6.4–10.6) in unvaccinated individuals and 3.7 (95% CI: 1.7–7.1) in fully vaccinated individuals. Incidence rates of seizure were 16.2 (95% CI: 13.6–19.3) and 0.8 (95% CI: 0.1–3.0), respectively. The IRRs for hospitalization and seizure in vaccinated versus unvaccinated individuals were 0.442 (95% CI: 0.195–1.000) and 0.190 (95% CI: 0.044–0.829), respectively.

Conclusion : COVID-19 vaccination was associated with reduced risks of hospitalization and seizure among children and adolescents during the Omicron period in Japan.

Antimicrobial resistance in E. coli bloodstream infections in Japan by age, sex, and region

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Introduction : *Escherichia coli (E. coli)* contributes substantially to Japan's antimicrobial resistance (AMR) burden, with increasing resistance prevalence and related mortality reported in recent years. Although age and sex influence AMR risk, most surveillance analyses do not incorporate these factors. Japan's hyper-aged population and robust national surveillance system offer a unique opportunity to explore how AMR risk varies demographically. This study aimed to assess variation in *E. coli* bloodstream infection (BSI) resistance by age, sex, and geography using data from the Japan Nosocomial Infections Surveillance (JANIS) system.

Methods : We extracted data on *E. coli* blood isolates submitted between 2008 and 2023 from the JANIS Clinical Laboratory division, covering approximately 25% of Japan's hospitals. Submissions were de-duplicated per WHO GLASS protocols. Susceptibility was classified using 2024 CLSI M100 MIC breakpoints. Multivariable logistic regression models estimated odds of resistance (binary outcome) by sex and age (5-year bands), adjusting for prefecture, ward type, hospital bed size, and year. Reference groups were males, age 84–85, and Tokyo prefecture. Models were built for cephalosporins, fluoroquinolones, and carbapenems.

Results : A total of 802,841 isolates were included. 644,271 were tested for cephalosporins and 744,476 for fluoroquinolones. Males generally had higher odds of AMR, but among patients aged 90+, females had greater odds for certain antibiotics, including cephalosporins (Odds Ratio (OR) 1.09, 95% Confidence Interval (CI): 1.02–1.15) and fluoroquinolones (OR 1.10, 95% CI: 1.03–1.17). Several prefectures, including Akita, Osaka, and Okinawa, showed elevated odds among females.

Conclusion : AMR risk varies by age, sex, and geography in Japan. The higher resistance in older females in specific regions may reflect social and structural factors, highlighting the need for gender- and age-sensitive AMR strategies as global populations age.