

**Trends in the Incidence of Disseminated Cryptococcosis in Japan: A Nationwide Observational study,**

**2015–2021**

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## Abstract

**Background:** *Cryptococcus* species can cause severe disseminated infections in immunocompromised hosts. This study investigated the epidemiological features and trends in disseminated cryptococcosis in Japan.

**Methods:** We used publicly available Infectious Diseases Weekly Reports to obtain data on the incidence of disseminated cryptococcosis in Japan from 2015 to 2021. Patient information, including age, sex, and regional and seasonal data, were extracted. The Joinpoint regression program was used to determine the age-adjusted incidence rate (AAR) per 100,000 population, annual percentage change (APC), and average APC (AAPC).

**Results:** A total of 1,047 cases of disseminated cryptococcosis were reported, of which those aged  $\geq 70$  years accounted for 68.8%. The AAR in men was significantly higher than that in women (median: 0.13 vs. 0.09;  $p=0.0024$ ). APC for the overall cases increased by 9.9% (95% confidence interval [95% CI]: -5.4 to 27.7) from 2015 to 2018 and then decreased by -3.3% (95% CI: -15.5 to 10.7) from 2018 to 2021. AAPC for the entire study period was 3.1% (95% CI: -1.5 to 8.0), indicating a possible increase in its number, although not statistically significant. In terms of regional distribution, the average AAR was highest in Shikoku District (0.17) and lowest in Hokkaido District (0.04). Northern Japan exhibited a significantly lower median AAR (median [interquartile range]: 0.06 [0.05, 0.08]) than the Eastern (0.12 [0.12, 0.13]), Western (0.11 [0.10, 0.13]), and Southern (0.14 [0.12, 0.15]) regions. No seasonal variation in incidence

was observed.

**Conclusion:** The prevalence of disseminated cryptococcosis has not increased in Japan. Geographically, the incidence is lower in Northern Japan. Further investigations that incorporate detailed clinical data are required.

**Keywords:** disseminated cryptococcosis; cryptococcal infection; epidemiology; trend analysis; regionality.