

Continued increase of multiple sclerosis and neuromyelitis optica in Japan; updates from the 5th nationwide survey

Short title: Updated epidemiology of MS and NMOSD in Japan

Noriko Isobe¹, Masaaki Niino², Takuya Matsushita¹, Yuri Nakamura^{3,4}, Ichiro Nakashima⁵, Mitsuru Watanabe¹, Yasunari Sakai⁶, Ayako Sakoda⁴, Jin Nakahara⁷, Izumi Kawachi⁸, Hirofumi Ochi⁹, Yuji Nakatsuji¹⁰, Yusei Miyazaki¹¹, Juichi Fujimori⁵, Kenji Kufukihara⁷, Tatsusada Okuno¹², Shoko Fukumoto¹, Fumie Hayashi¹, Kousuke Yonemoto⁶, Ryoji Taira⁶, Yosikazu Nakamura¹³, Koshi Nakamura¹⁴, Kiyomi Sakata¹⁵, Rinako Shimada¹, Makoto Matsui¹⁶, Jun-ichi Kira^{1,3,4}

¹Department of Neurology, Graduate School of Medical Sciences, Kyushu University, ²Department of Clinical Research, Hokkaido Medical Center, ³Translational Neuroscience Center, Graduate School of Medicine, and School of Pharmacy at Fukuoka, International University of Health and Welfare, ⁴Department of Neurology, Brain and Nerve Center, Fukuoka Central Hospital, International University of Health and Welfare, ⁵Department of Neurology, Tohoku Medical and Pharmaceutical University, ⁶Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, ⁷Department of Neurology, Keio University School of Medicine, ⁸Department of Neurology, Brain Research Institute, Niigata University, ⁹Department of Neurology and Geriatric Medicine, Ehime University Graduate School of Medicine, ¹⁰Department of Neurology, Toyama University Hospital, ¹¹Department of Neurology, Hokkaido Medical Center, ¹²Department of Neurology, Osaka University Graduate School of Medicine, ¹³Department of Public Health, Jichi Medical University, ¹⁴Department of Public Health and Hygiene, University of the Ryukyus, ¹⁵Department of Hygiene and Preventive Medicine, Iwate Medical University, ¹⁶Department of Neurology, Kanazawa Medical University

Backgrounds: In Japan, nationwide survey for multiple sclerosis (MS) has regularly been conducted since 1972, and the past 4 surveys conducted before the discovery of anti-aquaporin 4 antibodies.

Objective: To investigate the epidemiological characteristics of MS and neuromyelitis optica spectrum disorders (NMOSD) in Japan through the 5th nationwide survey.

Methods: Preliminary survey was conducted to ascertain the approximate number of patients with either MS or NMOSD who had seen at the selected facilities during 2017. Preliminary survey packages were sent to departments of neurology, internal medicine, ophthalmology, and pediatrics, at the facilities randomly selected using pre-determined sampling rates according to the stratification based on the number of hospital beds, as well as those specifically focused on these diseases. Secondary questionnaire was sent to the facilities which replied that they saw those patients in 2017 to collect the detailed clinical information of each patient.

Results: Response rates were 60.1% (2,284/3,799 departments) for preliminary survey and 53.5% (6,990/13,067 individual questionnaire forms) for secondary survey. Estimated number of MS and NMOSD patients were 24,118, which is more than 10-fold higher than that (2,280) of the 1st survey in 1972. The crude prevalence for MS and NMOSD was 19.6/100,000 (14.3 for MS and 5.3 for NMOSD). Male: female ratio was 1: 2.2 in MS and 1: 4.4 in NMOSD. The onset age (mean ± standard deviation, year) was 32.3±11.6 in MS and 44.2±16.1 in NMOSD. Proportion of ever-smokers were higher in MS compared to NMOSD (34.1% vs. 19.3%, $p = 2.5 \times 10^{-22}$). Disease-modifying therapy had been used for 75.4% in MS.

Conclusions: Compared to the previous survey, the prevalence of MS and NMOSD appears to be still increasing. Smoking could be a risk factor in Japanese MS as same as in other populations.

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