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Commentary

Regional and global perspectives on the incidence of multiple sclerosis and neuromyelitis optica and its spectrum disorders from Asia with emphasis on China

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CNS inflammatory disorders such as multiple sclerosis (MS), neuromyelitis optica/neuromyelitis optica spectrum disorders(NMO/NMOSD) are assuming increasing importance in recent years within Asia [1]. In *The Lancet Regional Health – Western Pacific*, De-Cai Tian and colleagues from China highlight important new data from two nationwide studies on MS/NMO/NMOSD for the first time giving the incidence of MS and NMO/NMOSD in children and adults as well as the burden of disease in terms of hospitalization duration, reimbursement and costs, mortality and common associated comorbidities rarely reported before [1,2].

The study encompasses one of the largest Asian populations sampled to date with better case ascertainments and inclusivity of paediatric and diverse populations. Both studies are large nationwide population-based studies on MS and NMO/NMOSD from a country that houses a fifth of the world's population. Tian et al. accessed information from the national database of the Hospital Quality Monitoring System (HQMS) that covers the entire Chinese population from mainly tertiary hospitals. The authors identified 1665 hospitals covering more than 90% of the tertiary public hospitals, with 11 973 newly diagnosed NMO/NMOSD patients and 9879 pts with MS from 2016–2018[1,2].

Though heterogeneity in methodology prevents head to head comparisons with other studies important points gleaned are as follows: their MS study is large by South-East/East Asian standards although smaller comparatively in absolute numbers than studies from West Asia, United States(US), Continental Europe and Oceania [3,4]. Their NMO/NMOSD study is one of the largest population-based NMO/NMOSD studies to date in terms of absolute numbers [1,2,5,7,8]. It is also noteworthy that this study was done post availability of Anti Aqp4 Ig G antibody testing and the IPND 2015 criteria for NMO/NMOSD resulting in better case ascertainment [5,7,8]. Further, Tian et al. reported the incidence of MS and NMO/NMOSD in both adults and children. There have been very few studies from within Asia and globally on paediatric MS/NMOSD.[6,7] In a recent meta-analysis, global paediatric MS incidence was 0.87 per 100,000 annually which is more than the current study [6,7]. A Japanese study on NMOSD reported rates of 0.06 per 100,000 in paediatrics which is comparable to Tian et al.'s current study [7].

Early global MS and NMO/NMOSD studies collected hospital/academic institution-based data within small regions in a country where case ascertainment was abstracted from standard diagnostic criteria. These were good starting points as regional population-based studies but rarely reflected nationwide data. Projecting estimates from one or a few regions to the entire country is of uncertain validity long-term. For instance, a local Malaysian study looking at a small region within the country underestimated the true occurrence of NMO/NMOSD within certain ethnic groups in the country leading to under-representation of cases within the Malay and Indian cohorts [8]. Though these efforts at reporting are commendable, it leads to conflicts in health care planning at a national level and unequal disease socio-demographic profiling. A similar nationwide study showed the prevalence of NMO/NMOSD amongst Malays, Chinese and Indians to be 0.9/0.9/0.6 per 100,000 (n=260/256/19) [9]. Therefore Tian et al.'s study utilizing the HQMS database, with careful case ascertainment is inclusive and comprehensive as it looks at all regions and increases relevance by covering a large population nationwide rather than extrapolating from a small region [1,2].

The estimated age and sex adjusted incidence for MS for all groups namely adults were comparable to other Asian reports wherein the overall incidence for MS ranged from 0.5 to 0.78

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per 100,000 in Malaysia, Taiwan, Japan and Korea respectively [1,2,3,4,9,10]. However, these rates though increasing are still low compared to high incidence areas in Western Asia like Iran where it is 3.4 per 100,000 and in the US, Europe, Scandinavia, Russia, Australia and New Zealand where it ranges from 1 to >10 per 100,000 [3,4,10]. This study is further substantiated by the recently published Atlas of MS 3rd Edition, where the prevalence of MS in China is reported to have doubled [3,4]. Thus, though the incidence is increasing in Asia, complex interactions between genetic susceptibility and the environment plausibly accounts for MS partiality to West Asia and Western populations [3,4].

Alternatively, the incidence of NMO/NMOSD in the present study is high and comparable to rates from Japan, Taiwan, Korea and Malaysia ranging from age adjusted 0.287 (adults:0.347 per 100,000) in China to 0.50–0.73 per 100,000 population in other South Asian countries. [1,2,8,9,10,11] These rates are higher than those reported in Caucasian studies but nearly comparable to Afro–American/Carribean reports [5,8].

Tian et al.'s study interestingly highlights the variability of NMO/NMOSD for certain ethnic groups, gender and regions within Asia with high NMO/NMOSD to MS ratios. The large numbers reported in their Chinese cohort is also seen in other Asian cohorts such as Malaysia where NMOSD is commoner amongst Chinese with NMOSD to MS ratios of 2:1 compared to Indians (MS:NMOSD 8.3:1) and Malays (MS:NMOSD 2:1) [9]. A recent Australia-New Zealand study also found Asians to be 3 times more prone for NMO/NMOSD than Caucasians [11]. Further, the authors identified a female predominance for both MS and NMOSD which is notably higher amongst their NMOSD patients i.e. 2.0:4.7 (MS: NMOSD). This female preponderance especially in NMOSD is also seen in other Asian MS and NMOSD studies from Japan, Korea, Hong Kong, Taiwan and Malaysia [5,9]. NMO/NMOSD studies from the US, Europe, Australia/New Zealand, West Asia and India also reveal a similar female predominance though less marked than East Asian studies [5,8,11].

Uniquely, Tian et al.'s study on MS reaffirmed the important effects of latitude seen in Japanese studies, and those from the US, Europe, Russia and Australia/New Zealand [3,4]. However, their study identified not only a negative north–south gradient but also a negative west–east altitude gradient not identified before for MS. This latitude preponderance was not seen in their NMOSD incidence study similar to reports from Australia/New Zealand thus suggesting other genetic factors in pathogenesis [1,2,11].

In terms of burden of disease, Tian et al.'s study reports mortality rates for MS and NMO/NMOSD of 6 to 7 per 1000 years and the occurrence of associated comorbidities such as hypertension in both conditions. Whilst autoimmune diseases such as SLE/Sjorgen syndromes are seen more with NMOSD than MS. In the past, mortality and morbidity has been scarcely explored in regional studies on MS/NMO/NMOSD [1,2]. The authors also assessed the burden of disease in terms of hospitalization costs, duration and associated comorbidities. This data is vital for budget impact analysis studies for health care planning and medication procurement regionally. Therefore, Tian et al.'s study on hospitalization burden and cost is timely to facilitate MS/NMO/NMOSD resource allocations more so with the advent of newer sophisticated disease modifying therapies, immunosuppressants and biologics for MS and NMO/NMOSD [1,2]. Additionally, their study reports the presence of a universal government based social health insurance which has successfully improved access to care for MS and NMOSD patients in China [1,2]. In summary, the authors provided important updated nationwide information on the epidemiology, burden and cost of disease from China with careful case ascertainment which shows similarities to other regional Asian studies and adds to current worldwide literature on MS and NMO/NMOSD.

Declaration of Competing Interest

The author has no conflicts of interest to report with regard to this commentary.

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