Epidemiology, Prevalence and Incidence of NMOSD at Penang Island, Malaysia, and a Review of Worldwide Prevalence and Genetic Associations

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OBJECTIVES

Unlike multiple sclerosis that is more prevalent in populations with European ancestry, AQP4-IgG+ NMOSD appears to be more prevalent among populations with non-European ancestry, suggesting certain degree of genetic predisposition. Several HLA and non-HLA genetic associations have been identified for NMOSD from studies in different ancestral groups.

While there were studies on changing incidence of multiple sclerosis over time, the temporal trend of NMOSD incidence (new cases) has not been extensively investigated. By studying the temporal trend in a specified population, it may provide insights into the "genetic vs. environmental" risk factors of the disease.

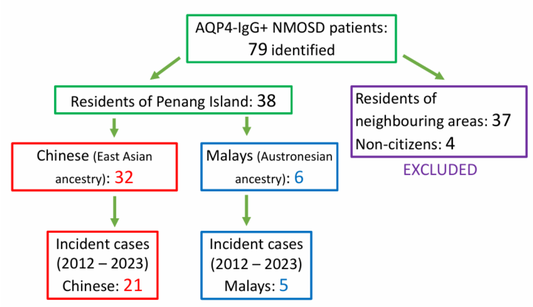
A population-based study was conducted to investigate the epidemiology, prevalence and the temporal trend of NMOSD incidence over 12 years (2012 – 2023) at Penang Island, Malaysia, located at the equatorial Southeast Asia.

METHODS

(1) Hospitals with neurology service (adult and paediatric) (n=6) at Penang Island participated in this study. Patients fulfilling the 2015 IPND criteria and were AQP4-IgG+ were included.

(2) Population-based prevalence studies and genetic studies of NMOSD worldwide were reviewed.

RESULTS



1. The prevalence of NMOSD is higher among people with East Asian ancestry than those with Austronesian ancestry or South Asian ancestry

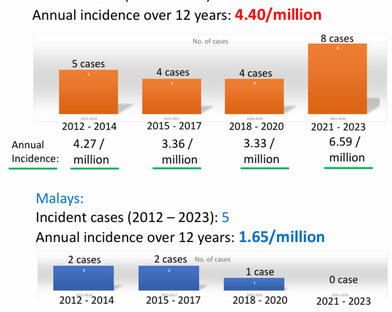
Prevalence Data: Prevalence Day: 31st Dec 2023

	No. of living patients	Prevalence Rate
Chinese (East Asians)	28	**6.96 / 100,000**
Malays (Austronesians)	4	**1.57 / 100,000**
Indians (South Asians)	---	

2. The incidence (new cases) of NMOSD appears relatively stable over the years, except for slight increase after universal Covid19 vaccination

Temporal trend of NMOSD incidence

Chinese:
Incident cases (2012 – 2023): 21
Annual incidence over 12 years: **4.40/million**

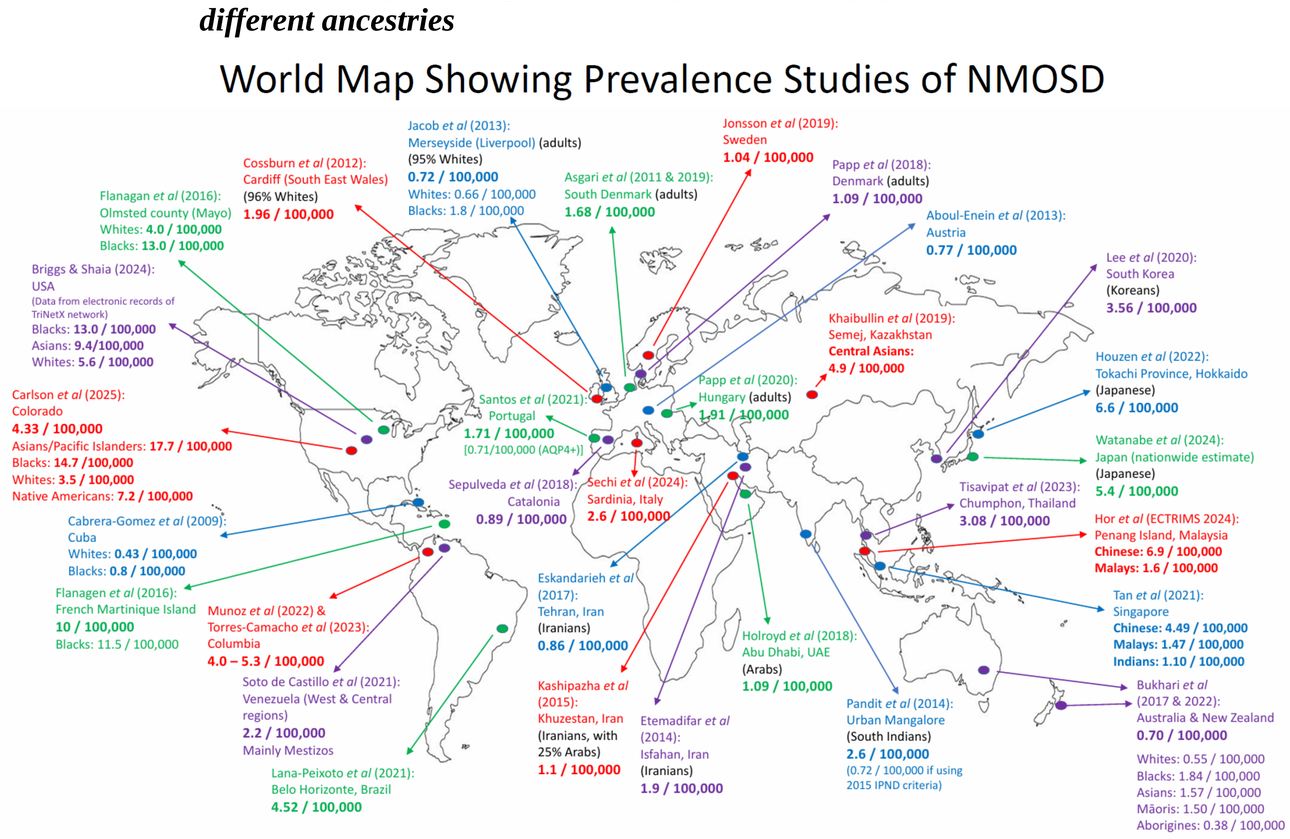


Malays:
Incident cases (2012 – 2023): 5
Annual incidence over 12 years: **1.65/million**

3. Vaccination acts as a minor trigger for NMOSD onset in at-risk population

The universal Covid19 vaccination in the whole island population in 2021-22 provides a unique opportunity to study the effect of vaccination on the disease onset. Among the Chinese population, in 2021-2023, 2 of the 8 incident cases had onset after Covid19 vaccination.

4. There is differential prevalence of NMOSD in populations with different ancestries



NO LATITUDE GRADIENT

Modified from Hor *et al*. Front Neurol 2020

Prevalence:
Whites / Europeans: ~2 / 100,000
Black Africans: up to 10 / 100,000
East Asians: ~6 / 100,000
Austronesians: ~2 / 100,000
South Asians: ~1 / 100,000
South America: 2.2 - 5 / 100,000
(With genetic contributions from African ancestry & Native American ancestry)

Annual incidence among:
Whites / Europeans: 0.37 – 1.32 / million
African-Caribbean: up to 7 / million
East Asians: ~ 3 – 4 / million
Austronesians: ~1.5 – 2 / million

5. Genetic studies identified several HLA risk and protective alleles in populations of various ancestries

Ancestral groups	Risk alleles	Protective alleles	
Asians:			
Chinese	DPB1*05:01 DRB1*16:02	DRB1*09:01	Wang *et al.*
Japanese	DPB1*05:01 DRB1*16:02 DRB1*08:02 DRB1*12 DQA1*05:03	DRB1*09:01	Isobe *et al.* Yoshimura *et al.* Matsushita *et al.* Ogawa *et al.*
Koreans	DRB1*03:01		Hyun *et al.*
Indians	DRB1*03		Pandit *et al.*
Arabs	DRB1*04:04 DRB1*10:01	DRB1*07 DQB1*02:02	Brill *et al.*
Other populations:			
Whites / Europeans	DRB1*03 A*01 B*08		Blanco *et al.* Estrada *et al.* Bruijstens *et al.* Tabansky *et al.*
Afro-Caribbeans	DRB1*03		Deschamps *et al.*
Brazilians	DRB1*03:01 DRB1*16:02 DRB1*04:05		Brum *et al.* Alvarenga *et al.* Kay *et al.*
Mexicans / Native Americans	DRB1*03 DRB1*10 DQB1*03:01 DRB1*08:02 DRB1*16:02 DRB1*14:06 DQB1*04:02	DQB1*03:02 DQB1*02:02	Alonso *et al.* Romero-Hidalgo *et al.*

Modified from Hor *et al*. Neurol Clin Neurosci 2021

CONCLUSIONS

Based on our and other population-based studies, there was differential prevalence of NMOSD in populations with different ancestries – Black African (up to 10/100,000), East Asian (~6/100,000), Austronesian (~2/100,000), European (~2/100,000) and South Asian (~1/100,000), despite some of them living in the same environment.

No latitude gradient was observed unlike that seen in multiple sclerosis.

The temporal trend of incidence (new cases) appeared relatively stable over time, apart from a slight increase after universal Covid19 vaccination.

Genetic studies in various populations identified several different HLA risk and protective alleles.

Genetic predisposition may play an important role in the disease prevalence and pathogenesis, and vaccination may be a minor trigger in at-risk population.