Short Communication

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Prevalence and direct costs of patients with neuromyelitis optica: data from Campania region in southern Italy

Emanuele Monda[‡,1], Stefano Iucolano[‡,2], Maria Galdo[2], Francesca Futura Bernardi[3], Paolo Chiodini[4], Daniela D'Angela[5], Roberta Giordana[6], Massimo Di Gennaro[7], Ugo Trama[5], Federico Spandonaro[8], Giuseppe Limongelli*[,§,1,2] & Barbara Polistena[§,8]

[1]Department of Translational Medical Sciences, Inherited & Rare Cardiovascular Diseases, University of Campania 'Luigi Vanvitelli', AO Colli – Monaldi Hospital, Naples, Italy

[2]Centro di Coordinamento Malattie Rare, Regione Campania, Italy

[3]General Direction of Health Care & Regional Health System Coordination, Drug & Device Politics, Campania, Italy

[4]Medical Statistics Unit, University of Campania 'L Vanvitelli', Naples, Italy

[5]CREA Sanità (Consortium for Applied Economic Research in Healthcare), Rome, Italy

[6]Regional Healthcare Society (So.Re.Sa), Naples, Italy

[7]ArSan Regional Health Agency of Campania Region, Naples, Italy

[8]Department of Economics & Finance, Faculty of Economics & Finance, University of Rome Tor Vergata, Via Columbia 2, Rome, 00133, Italy

*Author for correspondence: Tel.: +390 817 064 050; limongelligiuseppe@libero.it

‡Authors shared first name

§Authors shared last name

Aim: The study aimed to estimate the prevalence and direct costs of neuromyelitis optica (NMO) patients in Campania, Italy. **Materials & methods:** We retrospectively evaluated 53 NMO patients (mean age: 50.9 ± 16.5 years; 34% men) from the Campania Region administrative databases identified through disease exemption codes in 2018 and analyzed the incidence of NMO among the Campania region population and the disease-related cost. **Results:** The prevalence of NMO was 0.91 per 100,000 individuals. The average regional cost per NMO patient was 10,836.2 euros. The highest cost was related to drugs (60.6%), followed by hospitalizations (32.7%), diagnostics (4.8%) and laboratory tests (1.0%). **Conclusion:** NMO is an extremely rare disease with an annual disease-related cost of 0.005% of public health expenditure.

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Keywords: Campania region • costs of illness • epidemiology • Italy • neuromyelitis optica

Neuromyelitis optica (NMO) or Devic syndrome, is characterized by simultaneous or consecutive attacks of acute optic neuritis and transverse myelitis [1], caused by IgG autoantibodies to aquaporin 4 (AQP4-IgG) [2], or, less frequently, to myelin oligodendrocyte glycoprotein (MOG-IgG) [3]. NMO usually presents has a relapsing disease course without progression between attacks, which, if untreated, can lead to severe and persisting visual and motor dysfunction [4]. Medical treatment is based on high-dose glucocorticoids and plasma exchange for the acute phases and immunosuppressants for the long-term stabilization and prevention of attacks [5].

NMO is a rare condition with a prevalence ranging from 0.5 to four cases per 100,000 individuals [6–8]. Despite its low prevalence, it represents a significant public health concern for different reasons, such as the insufficient understanding of its etiology and pathophysiology, the absence of curative treatment, the frequent hospitalizations due to acute attacks and the attack-related disability. Indeed, given the disability that it produces, it is associated with elevated levels of healthcare and non healthcare resources. However, there is very little information on the economic impact of NMO.

The study aimed to estimate the prevalence and the disease-related costs of NMO patients in Campania (southern Italy).

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Table 1. Utilization of the main diagnostic procedures and other healthcare services due to neuromyelitis optica in 2018.

Diagnostic procedures and healthcare services	Total (n = 53)	<21 years (n = 3)	21–40 years (n = 12)	41–60 years (n = 22)	>60 years (n = 16)	p-value	Females (n = 35)	Males (n = 18)	p-value
Hospitalization	0.9 ± 1.3	0.7 ± 0.6	0.4 ± 0.4	1.1 ± 1.7	0.9 ± 1.1	0.875	1.1 ± 1.4	0.4 ± 0.9	0.088
Prescription drugs	66.4 ± 55.2	17 ± 6.1	25.2 ± 12.2	82.4 ± 82.3	84.6 ± 35.2	0.012	80.5 ± 70.3	39.1 ± 30.4	0.208
Diagnostics	4.1 ± 3.9	5.3 ± 4.2	4.4 ± 3.9	3.8 ± 3.6	4.2 ± 4.8	0.861	4.7 ± 3.9	2.9 ± 3.9	0.097
Laboratory analysis	22.3 ± 25.2	18.7 ± 17.6	20.3 ± 18.1	19 ± 25.6	29.1 ± 30.8	0.523	23.6 ± 25.0	20.5 ± 26.8	0.521
Physiotherapy	0.1 ± 0.5	-	-	-	0.3 ± 1.0	0.510	0.1 ± 0.7	-	0.498
Therapeutic	0.2 ± 0.6	-	0.5 ± 1.2	-	0.3 ± 0.6	0.204	0.2 ± 0.5	0.3 ± 1.0	0.629
Specialist visit	2.2 ± 0.7	2 ± 2.6	1.3 ± 1.3	2 ± 2.9	2.9 ± 3.3	0.804	2.7 ± 2.9	1.6 ± 2.3	0.231

The table reported the average diagnostic procedures and heath care services per NMO patient, according to age and sex.
NMO: Neuromyelitis optica.

Materials & methods

Study population & design

The study population comprised all patients with NMO from the Campania Region administrative databases in 2018, a regional database that collects cases from all the Campania region medical institutions which diagnose and manage patients with NMO. The diagnosis of NMO was formulated by neurologists specialized in the diagnosis and management of this rare condition according to the diagnostic criteria of a recent international expert consensus [9].

They were exempted from copayment under the protection of the healthcare services for NMO (exemption code 041.341.0). Prevalence may be underestimated because some patients chose not to apply for exemption, because of cultural or social reasons or because they already benefited from an income-based exemption, which generally offers a wider coverage for the health services used.

The analysis took into consideration the health-related consumption of the individuals benefiting from an exemption in 2018. The analyses used the interconnection of various regional administrative databases, thus making it possible to determine the amount of the public protection provided to NMO patients.

We retrospectively analyzed the prevalence of NMO among the Campania region population and the direct cost of NMO related to hospitalization, treatment, diagnostic procedures and other healthcare services, including in-patient and out-patient care.

Statistical methods

Normally distributed continuous data were described using means and standard deviation and compared using the Student *t*-test. Non-normally distributed data were described using medians and interquartile range and compared using Wilcoxon rank-sum and Kruskal–Wallis tests. Categorical data are presented as count divided by the total number of valid/available data and compared using Chi-square tests. Prevalence was calculated as the ratio between the number of patients with NMO and the population in Campania region in the year 2018, per 100,000 individuals, including the patients with NMO. Data were analyzed using R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria). A p-value of <0.05 (two-sided test) was considered significant.

Results

A total of 53 NMO patients (mean age: 50.9 ± 16.5 years; 34% men) were identified, with a prevalence of 0.91 per 100,000 individuals in the Campania region. The prevalence was greater in women than in men males (1.2 per 100,000 and 0.65 per 100,000 individuals, respectively).

The regional average cost per NMO patient is equal to 10,836.2 euros, which is 4883.4 euros higher than the average regional cost for rare disease patients. Total expenditure amounts to 533,400 euros, equal to 0.005% of public healthcare region spending. The highest cost is related to drugs (60.6% of total expenditure; in particular, 42.7% for immunosuppressives, 20.9% for immunostimulatory, 6.8% for antiviral ones), followed by hospitalizations (32.7%), diagnostics (4.8%) and laboratory tests (1.0%). Use and cost-related diagnostic procedures and other healthcare services are presented in Tables 1 & 2, respectively.

Drug-related costs

In 2018, the average prescription drugs per NMO patient was 66.4 with an average cost of 6101.3 euros per NMO patient (Table 2). The higher number of prescription drugs was observed in NMO patients ≥41 years

Table 2. Average cost of the main diagnostic procedures and other healthcare services due to neuromyelitis optica in 2018.

Diagnostic procedures and healthcare services	Total (n = 53)	<21 years (n = 3)	21–40 years (n = 12)	41–60 years (n = 22)	>60 years (n = 16)	p-value	Females (n = 35)	Males (n = 18)	p-value
Hospitalization	3290.3 ± 7514.6	788.7 ± 685.9	202.2 ± 259.2	5178.8 ± 11576.2	3478.8 ± 5763	0.697	4190.5 ± 8661.3	1540 ± 4421.3	0.110
Prescription drugs	6101.3 ± 5123.5	10280.9 ± 6899.4	8379.5 ± 6423.4	5925.3 ± 4675.4	3851.2 ± 3529.6	0.801	5921.4 ± 4783.3	6451.3 ± 4323.2	0.998
Diagnostics	470.1 ± 437.6	776.7 ± 467.6	668.1 ± 610.7	429.1 ± 379.1	320.5 ± 280.8	0.138	496.5 ± 410.9	451.6 ± 502.4	0.164
Laboratory analysis	96.8 ± 116.6	78 ± 68.3	78,2 ± 83.4	84.6 ± 103.7	166.9 ± 161.0	0.492	106.8 ± 131,9	75.8 ± 83.4	0.473
Physiotherapy	17.2 ± 125.6	-	-	-	57.1 ± 228.2	0.510	26.1 ± 154.3	-	0.498
Therapeutic	8.5 ± 41.1	-	29.3 ± 85.4	1,5 ± 7.3	4.1 ± 9.2	0.228	3.8 ± 9.9	17.7 ± 70.2	0.640
Specialist visit	70.9 ± 43.2	29 ± 34.2	35.8 ± 22.8	99.1 ± 54.7	66.3 ± 53.0	0.817	87.4 ± 47.7	39.1 ± 32.3	0.266

The table reported the average cost of the diagnostic procedures and heath care services per NMO patient, according to age and sex.
NMO: Neuromyelitis optica.

old (17 ± 6.1 in those <21 years old, 25.2 ± 12.2 in those 21–40 years old, 82.4 ± 82.3 in those 41–60 years old and 84.6 ± 35.2 in those >60 years old; p-value: 0.012). However, no significant difference was observed in the number of prescription drugs in men compared with women and in average costs for prescription drugs among the different classes of age and sex.

Hospitalization-related costs

In 2018, the average hospitalization per NMO patient was 0.9 and the average hospitalization-related costs were 3290.3 euros per NMO patient (Table 2). Compared with men, a higher but not statistically significant prevalence both of the average hospitalization and hospitalization-related costs per NMO patient was seen in women (1.1 ± 1.4 vs 0.4 ± 0.9, p-value: 0.09; 4,190.5 ± 8,661.3 vs 1,540 ± 4,421.3 euros, p-value: 0.11). No significant difference occurred among the different classes of age.

Of the 37.7% of all patients hospitalized, 40% were admitted for non life-threatening problems and 60% for day hospital (DH).

Other healthcare-related cost

In 2018, the average diagnostic procedures, laboratory analysis, physical therapy, therapeutic procedures and specialist visit per NMO patients were 4.1 ± 3.9, 22.3 ± 25.2, 0.1 ± 0.5, 0.2 ± 0.6 and 2.2 ± 0.7, respectively. Among these, diagnostic procedures represented the highest average cost per NMO patient, equal to 470.1 ± 437.6 euros. No significant difference was seen among sex or classes of age.

For NMO patients, 69.8% received visits and diagnostic work ups, 66% had laboratory analyses, 15.1% underwent treatment and 1.9% helped by rehabilitation services.

Discussion

Our study provides data on prevalence, healthcare utilization and costs of patients with NMO in an Italian region based on the data collected from the Campania region administrative databases in 2018. This is the first study to describe the prevalence of NMO in an Italian region. Similar to that reported in other countries, which ranges from 0.5 to four cases per 100,000 individuals [6–10], the prevalence of NMO in Campania region was 0.91 per 100,000 individuals, with an higher prevalence of women than men.

According to the natural history of NMO, patients experience several relapses during life, resulting in unpredictable and cumulative neurologic disabilities and no treatment has been found to be effective in prospective and adequately powered clinical trials. Therefore, NMO has negative effects on patients' quality of life, in particular concerning physical disability, pain, bowel and bladder dysfunction and visual impairment [11–13]. The decreased quality of life impacts significantly on anxiety, disability and depression NMO patients.

Thus, NMO patients were managed with and without drugs to control the acute attacks, for long-term stabilization and prevention of relapses. Furthermore, NMO patients underwent an elevated number of diagnostic procedures and hospitalization, which contribute to the reduced quality of life and the increased economic burden of this condition.

In this study, the annual regional average cost per NMO patient was 10,836.2 euros, mostly related to medications, followed by hospitalization and diagnostic procedures. These data are consistent with a previous study of NMO patients in North America, which showed that the most frequently reported cost was related to prescription medication and hospitalization [13].

However, some limitations should be acknowledged. The most important limitation is related to the study design, which follows a database-based instead of a population-based approach. Moreover, this study evaluated only the direct costs, related to drugs, hospitalization, diagnostic procedures and other healthcare services, while indirect costs (e.g., productivity loss and informal care) and intangible costs (e.g., deterioration in the quality of life of patients, their family and friends) has not been assessed. Finally, this evaluation was done before the approval of several novel NMO drugs, which are much more expensive than conventional immunosuppressant; thus, this study may underestimate the real disease-related costs.

Conclusion

NMO is a rare autoimmune condition characterized by unpredictable relapses that affect the optic nerves and spinal cord, which can lead to severe and persisting visual and motor dysfunction. This study confirmed the extremely rarity of this condition showing a prevalence of 0.91 per 100,000 individuals in Campania region. Moreover, it represents a significant public health concern, exhibiting an annual disease-related cost of 0.005% of public health expenditure in Campania region.

Summary points

- The regional average cost per neuromyelitis optica (NMO) patient is equal to 10,836.2 euros, which is 4883.4 euros higher than the average regional cost for rare disease patients.
- The average prescription drugs per NMO patient was 66.4 with an average cost of 6101.3 euros per NMO patient. The higher number of prescription drugs was observed in NMO patients ≥41 years old.
- The average hospitalization per NMO patient was 0.9 and the average hospitalization-related costs were 3290.3 euros per NMO patient.

Author contributions

E Monda, S Iucolano, G Limongelli and P Barbara contributed to the conception and design of the work. M Di Gennaro, FF Bernardi, P Chiodini, D D'Angela, R Giordana, M Di Gennaro, U Trama and F Spandonaro contributed to the acquisition, analysis or interpretation of data for the work. E Monda, S Iucolano, G Limongelli and P Barbara drafted the manuscript. All the authors critically revised the manuscript, gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Financial & competing interests disclosure

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

Our research protocol adheres to the principles of the Declaration of Helsinki and its amendments and has been approved by the Ethics Committee of our institution. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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