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Análise epidemiológica da doença do neurônio motor em um serviço de referência em neurofisiologia clínica no Brasil

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Epidemiological Analysis of Motor Neuron Disease in a Clinical Neurophysiology Reference Service in Brazil

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Abstract

Background and Purpouse: The present study presents a retrospective assessment of an electroneuromyography studies database performed in a clinical neurophysiology reference service in the Triângulo Mineiro and Alto Paranaíba region of Minas Gerais state in Brazil, performing a detailed epidemiological evaluation of motor neuron disease in the context of a reference service.

Methods: A retrospective design has been employed, analyzing aggregate data from 20 patients submitted to ENMG on suspicion of MND in our service, within a sample universe of 909 tests performed during 2 years. Patients were stratified according to initial symptomatic manifestation (pre-testing probability) and ENMG electrophysiological verdict. The correlation between pretest probability (defined by clinical presumption with referral indicating the suspicion) and diagnostic confirmation and the correlation between the diagnostic criteria of El Escorial and Awaji and Gold Coast.

Results: An annualized incidence of 1,24% was observed for MND in this setting, higher than the incidence observed in the general population (0,002%). The analysis revealed a Positive Predictive Value (PPV) of 65% for the clinical suspicion alone.

Conclusion: The markedly higher incidence of MND observed in our ENMG reference center, compared to the general population, reflects the intrinsic selection bias of specialized diagnostic services, where exams are performed exclusively on patients with clinical suspicion of neuromuscular disorders. A higher PPV may suggest delayed referrals, with patients being sent only when clinical suspicion is already high and disease is more advanced, whereas a lower PPV could indicate earlier referrals, potentially improving patient outcomes.

Keywords: Motor Neuron Disease (MND); Electroneuromyography (ENMG); Amyotrophic Lateral Sclerosis (ALS); Diagnostic accuracy; Epidemiology.

Introduction

Motor neuron disease (MND) comprises a large phenotypic group of pathologies, with multiple and diverse initial pathophysiological mechanisms, which inexorably converge on the impairment and progressive degeneration of lower and/or upper motor neurons^{1,2,3}.

It is a neurodegenerative disease with high morbidity and mortality, considered a rare disease by the concept of the World Health Organization and GM/MS Ordinance No. 199, of January 30, 2014, of the Brazilian Ministry of Health⁴.

Existing treatments are currently based mainly on multidisciplinary care and pharmaceuticals that do not aim on curing the disease, but rather try to contain its rapid progression. In this context, there is currently a great effort for the prompt recognition and early diagnosis of pathology, with an objective of including more patients for clinical trials studying new treatments (which includes not only new drugs, but also combination of drugs and novel delivery routes), during the initial phases of the disease.

The heterogeneous clinical presentation of the DNM and the existence of various conditions that simulate their symptoms make the diagnosis a complex clinical challenge. Electroneuromyography (ENMG) is an indispensable diagnostic tool for the accurate diagnosis of DNM, being essential not only for the investigation of differential diagnoses, but also for detecting lower motor neuron disease with a higher sensitivity in the early stages.

This study aimed to evaluate the correlation between the pre-test probability of MND and the post-ENMG diagnostic confirmation in a reference service in the Triângulo Mineiro and Alto Paranaíba region of Minas Gerais state, in Brazil, seeking to analyse the accuracy of clinical suspicion as a main tracking tool for the cases. We also aimed to quantify the incidence of MND in the context of an Electroneuromyography laboratory / Neuromuscular clinic and discuss the role of the Gold Coast diagnostic criteria compared to the earlier El Escorial and Awaji criterias⁵⁻¹⁰.

Declarations

This study is based solely on the retrospective analysis of ecological, aggregated data derived from the routine operation of a private healthcare company contracted to perform Electroneuromyography (ENMG) for the public health sector. The dataset contains no individual-level information, personal identifiers, or sensitive data, and does not involve any experimental intervention, manipulation, or recruitment of human or animal subjects. The research ethics committee, authorization n°2025.1.4.007 - CEP/VIRTUS ENMG/Uberaba/MG/Brazil.

All data used in this study are anonymized and aggregated at a population level, rendering it impossible to identify individual patients. No clinical trials, behavioral interventions, or animal testing were conducted. The study does not access medical records in a manner that would allow the re-identification of subjects, nor does it involve interaction with patients or the collection of primary data.

As such, this research qualifies as exempt from Institutional Review Board (IRB) or Institutional Animal Care and Use Committee (IACUC) oversight, in accordance with international and national ethical guidelines for research involving humans and animals. Furthermore, there are no conflicts of interest to disclose, as the authors are independent of the healthcare provider company and have no financial or proprietary interest in the data.

Methods

Study Design: We conducted a retrospective study of aggregate data collected in electroneuromyography examinations in a reference service for neuromuscular diseases to evaluate diagnostic performance.

Study site: The data were collected from the private practice services of Dr. Luis Marcos Ferreira Junior, located in the cities of Uberaba/MG and Araxá/MG, both in the Triângulo Mineiro and Alto Paranaíba region of Minas Gerais state in Brazil.

Study population: All patients referred to the ENMG clinic. Data collection covered the period from March 1st of 2023 to February 28th of 2025, using records of electronic medical records and exam reports.

Variables and definitions:

Pretest Probability: Categorized based on the presence or absence of highly suggestive clinical symptoms, as documented in the patient's referral and clinical history.

With symptoms (High pre-test probability):

1. Documented progressive weakness;
2. Clinical signs of involvement of the second motor neuron (muscle atrophy, fasciculations, hypo/border);
3. Clinical signs of involvement of the first motor neuron (signs of pyramidal release, spastic stiffness, clonus, hyperreflexia);
4. Semiotic absence of signs and symptoms which would make other diagnoses more likely.

Post-EMG Confirmation: MND diagnosis was considered confirmatory when electrophysiological findings were compatible with MND diagnostic criteria (revised Goldcoast criteria and/or EL Scores and Awaji together⁵⁻¹⁰) and other differential diagnoses were considered ruled out.

Results

Electroneuromyography tests were performed at 909 patients in the service during the period from March 1st of 2023 to February 28th of 2025.

Among these, 20 patients had the prior clinical suspicion of MND (2.19% of the population referenced to the service), and 13 of these patients had their diagnoses confirmed with

the help of electroneuromiography (defining an annualized incidence of 1,24% of the total population and a 65% diagnostic confirmation rate in the evaluated period).

In addition to these cases, there was an initial clinical suspicion of MND by the clinical neurophysiologist (without prior suspicion by the requesting physician) during the clinical evaluation performed previously to electroneuromyographic examination and/or during electroneuromiographic study in 6 patients (0.66% of the total population excluding patients with external prior suspicion) with subsequent diagnostic confirmation in 2 patients. These patients did not enter the calculation of the positive predictive value, however, due to the obvious selection and confirmation biases involved, in order to maintain the reliability of the study.

Through this, the calculation of the positive predictive value of the initial clinical suspect performed by the assistant doctors was made:

(Table 1)

It was also possible to calculate the positive predictive value of the initial clinical suspicion made by the clinical neurophysiologist on patients referred without the previous suspicion made by the referring doctor. This data, as previously stated, was separated from the main analysis due to the not meeting the quality eligibility criteria of this study (due to the clinical evaluator and EMG performer being the same person):

(Table 2)

The following are the final epidemiological data obtained:

(Table 3)

Discussion

We must primarily state that the incidence of MND in the general population is low, with estimates varying globally. According to a systematic review and meta-analysis published in the Journal of Neurology, Neurosurgery & Psychiatry (JNNP) in 2021, the annual incidence of Amyotrophic Lateral Sclerosis (ALS), the most common form of DNM, ranges from 0.6 to 3.8 cases per 100,000 people/year in western populations^{2,4,5}. In contrast, in specialized reference centers with ENMG laboratories, where the diagnoses of MND is

confirmed, the incidence of the disease tends to be significantly higher, with a study published in the *Journal of Clinical Neurosciences (JNC)* in 2023 showing an incidence rate as high as 4,3% in a tertiary care center in the Philippines.

In our service, with a sample universe of 909 ENMG tests performed during the period of two years, we confirmed 4 cases out of 230 in the period of 2023 and 9 cases out of 679 in 2024. In total, 13 cases were confirmed as MND. This represents an annualized average incidence of 1.24%. By comparison, the incidence rate in our ENMG service is approximately 327 to 2075 times higher than the incidence of the general population (1.24% vs. 0.0038% to 0.0006%), considering the previously referenced study by JNNP^{9,11}.

The high incidence in the context of a neuromuscular reference service / ENMG laboratory reflects the higher pre-test probability the patients of the service will have, once ENMG is exclusively a diagnostic tool, not being routinely used in patients who do not present clinical symptoms of peripheral nervous system impairment. It remarks the service's function as a diagnostic pole for specific neurological pathologies rather than a mere indicator of population prevalence.

This metric, though, could arguably be used to track and evaluate the quality of healthcare services in a region. In poorer places, with limited access to the ENMG exam, the incidence would tend to be higher than in places where the study is done in more people with less serious symptoms and earlier. Concomitantly, the Positive Predictive Value of the clinical suspicion could also arguably be used to assess the quality of referencing healthcare services, wherein a higher PPV could mean that people are being referenced for ENMG evaluation in a later stage of the disease, rather than being referenced when the clinical symptoms are still less prominent and therefore differential diagnoses are still likely to be considered.

Nevertheless, there are some important biases involved in using those metrics purely without critical thinking. The quality of an ENMG examiner / ENMG service is a sensible bias to that measurement, once the detection rate would drop in the setting of a poorly executed exam, underestimating the detected incidence. Another important factor is that a lower PPV could not only reflect an earlier clinical suspiciousness rate by the referencing services, but also, an oppositely negative tendency of suspecting MND in cases where a thorough clinical examination would rule out that possibility, despite its semiotic distinctiveness.

The clinical diagnosis of this pathology is traditionally based on structured criteria, such as the criteria of El Escorial (1994, revised in 2000) and subsequently included the criteria of Awaji (2008)⁵⁻¹⁰. Both of current use but with important limitations, mostly being criticized for its complexity and necessity for a more widespread disease to conclude the diagnosis. The Gold Coast criteria, proposed in 2019, emerged with the explicit objective of simplifying the diagnostic process and increasing sensitivity, especially in the early stages of the disease. Unlike El Escorial and Awaji, which require a more rigorous and topographic combination of clinical signs of involvement of the upper and lower (NMI)

motor neurons in multiple body regions, Gold Coast criteria are based on a more direct and pragmatic approach^{9,11}. The central focus was to allow doctors to be able to establish the diagnosis with less variables, in an attempt to reduce the time between the onset of symptoms and diagnostic confirmation.

In a brief overhaul of literature, addressing recent studies and comparative meta-analyses, published in the PubMed database, it is clear that the EI Escorial criteria are of high specificity, however their sensitivity can be as low as 30–50% in the first 12 months of symptoms. Awaji's criteria, by incorporating more aggressively electrophysiological findings, improved this sensitivity to about 60–70%, but still maintained interpretative complexity.

(Table 4)

These studies confirm that Gold Coast criteria reach greater sensitivity, facilitating early diagnosis. Specificity remains adequate for the inclusion of patients in research, although it is slightly lower than that of EI Escorial/Awaji in some scenarios.

Out of all the confirmed cases, we found that only 61,5% of them reached a final diagnosis with both Awaji and Gold Coast criteria, with 38,5% of the cases reaching the final diagnosis only by the Gold Coast criteria. This final data found in our study confirms how much more sensible the Gold Coast criteria is for detecting MND in earlier stages.

Even though MND is a challenging disease with an irreversible progression, an early and accurate diagnosis can help in the prognostic definition for patients, allowing them to plan their care and prevent dysthanasia. Also, even if modestly, the quality of life and survival rates can also be significantly improved through interventions such as the readily available drug therapies and multidisciplinary management, with nutritional care, respiratory and physiotherapy and ventilation assistance, dysphagia and speech therapy and psychological follow up.

In any case, it is important to highlight that the objective of the implementation of Gold Coast criteria was not solely the improvement of final clinical outcomes, but also to enable more patients to be selected and included in clinical trials for new treatments. The accurate diagnostic confirmation is imperative for eligibility in clinical trials, which tend to include mostly patients within the early stages of the disease. There is not only an active search for new substances that may improve morbimortality in MND, but also new approaches to previously tested substances. The use of different substances in combination, such as the sodium phenylbutirate-tauroursodeoxycholic acid, have been approved for MND/ALS treatment by the American Food and Drug Administration (FDA) in 2022,⁹⁻¹². Alternatively, the testing of different delivery routes for known substances is also an effort scientists are doing to try to improve MND treatment.

To summarize and conclude, both incidence within the service and the positive predictive value (PPV) of clinical referrals could serve as indirect indicators of healthcare quality. A higher PPV may suggest delayed referrals, with patients being sent only when clinical suspicion is already high and disease is more advanced, whereas a lower PPV could indicate earlier referrals, potentially improving patient outcomes but also posing risks of over-referral if not clinically justified. However, interpreting these metrics requires caution, as they are heavily influenced by factors such as the availability of ENMG, the expertise of examiners, and the quality of the initial clinical assessment. In regions with limited access to specialized exams, incidence and PPV could paradoxically be higher due to late-stage diagnoses, whereas in systems with broader access, these rates may decrease as patients are evaluated earlier in the disease course.

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Epidemiological Analysis of Motor Neuron Disease in a Clinical Neurophysiology Reference Service in Brazil

Tables and figures

- Table 1

	ENMG Confirmed for MND	ENMG not Confirmed for MND	Total
with Symptoms (High pré-teste prob.	13 (True positives)	7 (False Positives)	20

- Positive predictive value: $13 / (13 + 7) = 65\%$.

- Table 2

	ENMG Confirmed for MND	ENMG not Confirmed for MND	Total
with Symptoms (High pré-teste prob.	2 (True Positives)	4 (False positives)	6

- Positive predictive value: $2 / (2 + 4) = 33,3\%$

- Table 3

Incidence/year of patients referred to the clinic with suspected MND* (March 2023 to February 2025)	2,19%
Incidence/year of MND confirmed with the help of electroneuromyography** (March 2023 to February 2024)	1.17%
Incidence/year of MND confirmed with the help of electroneuromyography** (March 2024 to February 2025)	1.32%
Average incidence/year of confirmed MND**	1.24%
Positive predictive value of initial clinical evaluation	65%

* Included patients who did not obtain the confirmation of the diagnosis, considering only suspicions performed by the assistant doctors previously to the exam

** Excluded cases diagnosed without the prior suspicion of the assistant doctor

- **Table 4**

Main indicators (references 8, 9,10 e 11)

Criteria	Sensibility	Especificity
Awaji vs. rEEC	↑ 57% vs. 45%	= 99,5% (both)
Gold Coast vs rEEC/Awaji	96,6% > 85% (rEEC/Awaji)	Slightly higher

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