

Demographic factors associated with cognitive impairment in patients with relapsing-remitting multiple sclerosis: BICAMS battery analysis

Factores demográficos asociados con el deterioro cognitivo en pacientes con esclerosis múltiple remitente-recurrente: análisis de la batería BICAMS

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ABSTRACT

Introduction: Multiple sclerosis is a chronic, immune-mediated disease of the central nervous system that frequently leads to cognitive decline, significantly impacting patients' quality of life and functionality. Understanding how demographic variables interact with cognitive performance is essential to guide clinical evaluation and therapeutic strategies. **Objective:** To determine the relationship between demographic factors and cognitive impairment in patients with relapsing-remitting multiple sclerosis at the Teodoro Maldonado Carbo Hospital, Guayaquil-Ecuador, 2017-2022. **Methods:** A correlational, non-experimental, descriptive study that included 145 patients with relapsing-remitting multiple sclerosis. Demographic factors (age, sex, level of education) and cognitive impairment were evaluated using the BICAMS (Brief International Cognitive Assessment for Multiple Sclerosis) battery. Pearson's Chi² tests was used to establish statistical relationships. **Results:** The mean age was 40.75±13.46 years, with a slight female predominance (52%). Cognitive impairment occurred in 6.2-10.3% depending on the domain evaluated. A statistically significant association was found between age and cognitive impairment measured by BVMTR ($p=0.007$). The level of schooling showed a significant association with BVMTR ($p<0.001$) and CVLT-II ($p=0.033$). No significant association between sex and cognitive impairment was observed in any test ($p>0.05$). **Conclusions:** Demographic factors age and level of education are significant predictors of cognitive impairment in patients with relapsing-remitting multiple sclerosis, while sex showed no association. These findings suggest the importance of considering cognitive reserve in neuropsychological assessment.

Keywords: multiple sclerosis, cognitive impairment, BICAMS, demographic factors, cognitive reserve.

Palabras clave:

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RESUMEN

Introducción: La esclerosis múltiple es una enfermedad crónica e inmune-mediada del sistema nervioso central que con frecuencia conduce al deterioro cognitivo, impactando de manera significativa en la calidad de vida y la funcionalidad de los pacientes. Comprender cómo las variables demográficas interactúan con el desempeño cognitivo resulta esencial para orientar la evaluación clínica y las estrategias terapéuticas. **Objetivo:** Determinar la relación entre los factores demográficos y el deterioro cognitivo en pacientes con esclerosis múltiple remitente-recurrente del Hospital Teodoro Maldonado Carbo, Guayaquil-Ecuador, 2017-2022. **Materiales y métodos:** Estudio descriptivo correlacional, no experimental, que incluyó 145 pacientes con esclerosis múltiple remitente-recurrente. Se evaluaron factores demográficos (edad, sexo, nivel de escolaridad) y deterioro cognitivo mediante la batería BICAMS (Brief International Cognitive Assessment for Multiple Sclerosis). Se utilizó la prueba Chi² de para establecer rasociaciones estadísticas. **Resultados:** La edad media fue 40.75±13.46 años, con ligero predominio femenino (52%). El deterioro cognitivo se presentó en 6.2-10.3% según el dominio evaluado. Se encontró asociación estadísticamente significativa entre la edad y el deterioro cognitivo medido por BVMTR ($p=0.007$). El nivel de escolaridad mostró asociación significativa con BVMTR ($p<0.001$) y CVLT-II ($p=0.033$). No se observó asociación significativa entre sexo y deterioro cognitivo en ninguna prueba ($p>0.05$). **Conclusiones:** Los factores demográficos edad y nivel de escolaridad constituyen predictores significativos del deterioro cognitivo en pacientes con esclerosis múltiple remitente-recurrente, mientras que el sexo no mostró asociación. Estos hallazgos sugieren la importancia de considerar la reserva cognitiva en la evaluación neuropsicológica.

Palabras clave: esclerosis múltiple, deterioro cognitivo, BICAMS, factores demográficos, reserva cognitiva.

INTRODUCCIÓN

Multiple sclerosis (MS) is a chronic neurodegenerative disease of the central nervous system that affects approximately 2.8 million people worldwide (1). This autoimmune pathology is characterized by processes of demyelination and inflammation that lead to a wide range of clinical manifestations, among which cognitive impairment (CI) represents one of the most prevalent and disabling complications (2).

CI in MS affects between 32.5% and 44% of patients, depending on the diagnostic criteria and assessment tools used (3-4). This neuropsychological compromise significantly impacts patients' activities of daily living, work functioning, social relationships, and overall quality of life (5). The most frequently affected cognitive domains include information processing speed, episodic memory, executive functions, and working memory (6).

The systematic assessment of cognitive functioning in MS has acquired special relevance in recent years, particularly with the development of specific tools such as the BICAMS (Brief International Cognitive Assessment for Multiple Sclerosis) battery (7). This battery, internationally validated, allows an efficient and standardized assessment of the most vulnerable cognitive domains in MS, facilitating its implementation in routine clinical practice (8).

Demographic factors have emerged as important predictors of cognitive decline in MS. Age is a well-established risk factor, with studies demonstrating a higher prevalence of CI in older patients (9). Educational level, on the other hand, has been identified as a protective factor through the concept of cognitive reserve, where higher educational levels are associated with greater resistance to CI (10). As for sex, the results have been less consistent, with some studies reporting differences while others find no significant associations (11).

In the Latin American context, and particularly in Ecuador, evidence on the relationship between demographic factors and cognitive impairment in MS is limited (12). Previous studies in the country have focused mainly on general epidemiological aspects, without delving into the specific analysis of cognitive functioning and its determinants (13). This gap in scientific knowledge justifies the need for research that specifically addresses the relationship between demographic variables and CI in Ecuadorian populations with MS.

Understanding these predictors is crucial for the development of early intervention strategies, personalized cognitive rehabilitation programs, and public health policies aimed at improving the functional prognosis of patients with MS (14). In addition, knowledge of these determinants allows for the optimization of diagnostic and therapeutic resources, focusing attention on populations at higher risk.

The objective of this study was to determine the relationship between demographic factors (age, sex, and level of education) and cognitive impairment in patients with relapsing-remitting multiple sclerosis (RRMS) at the Teodoro Maldonado Carbo Hospital in Guayaquil, Ecuador, during the period 2017-2022, using the BICAMS battery as a neuropsychological assessment tool

MATERIALS AND METHODS

Study design and population

A relational descriptive study was conducted, based on a non-experimental and cross-sectional design. The study population consisted of patients diagnosed with RRMS treated at the Teodoro Maldonado Carbo Hospital in Guayaquil, Ecuador, during the period 2017-2022.

Sample and selection criteria

Out of a total of 170 patients registered with RRMS, 145 participants were selected who met the inclusion criteria. The inclusion criteria were: (a) confirmation of the diagnosis of RRMS issued by a hospital neurologist; (b) age ≥ 18 years and proficiency in the Spanish language; (c) complete BICAMS and EDSS assessment data; (d) neurological stability for at least 4 weeks prior to evaluation. Exclusion criteria included: (a) incomplete BICAMS or EDSS data; (b) psychiatric or neurological comorbidity; (c) depression according to the Beck Inventory < 13 points; (d) uncorrected hearing or visual problems; (e) a history of learning disorders; (f) drug use.

Variables and measurements

Demographic variables: data on age (in years), sex (male/female) and level of schooling (basic, secondary, baccalaureate, higher, fourth level) were considered.

Cognitive assessment: the BICAMS battery was used, which includes three subtests: (1) Symbol Digit Modality Test (SDMT) to evaluate information processing speed and working memory; (2) California Verbal Learning Test-II (CVLT-II) to measure long-term verbal learning and memory; (3) Brief Visuospatial Memory Test-Revised (BVMTR) to assess visuospatial learning and memory⁷.

Cognitive impairment criteria: CI was defined as scores below the 5th percentile on at least 20% of BICAMS tests, based on established criteria (15).

Statistical analysis

A descriptive analysis was performed using frequencies, percentages, means and standard deviations (SD) and confidence intervals (IC: 95%). For the inferential

analysis, Pearson's Chi² tests (α : $p < 0.05$) were used for categorical variables. Effect size (ES) was calculated according to Cohen's criteria and statistical power (P : $1 - \beta$). The analyses were performed in SPSS v.26 and R Studio.

Ethical considerations

The study was approved by the Ethics Committee of the Teodoro Maldonado Carbo Hospital, following the principles of the Declaration of Helsinki. All participants signed informed consent.

RESULTS

Demographic characteristics of the sample

The final sample included 145 patients with RRMS, with a mean age of 40.75 ± 13.46 years (IC 95%: 38.56-42.94). The distribution by sex showed a slight female predominance with 75 women (52%) vs. 70 men (48%). In relation to the age distribution, 29.9% ($n=46$) were ≤ 30 years old, 24.7% ($n=38$) were between 31-40 years old, 20.8% ($n=32$) were between 41-50 years old, 18.2% ($n=28$) were between 51-60 years old, and 6.5% ($n=10$) > 60 years old (Table 1).

Table 1

Demographic characteristics of the sample (n=145)

Variable	Category	n	%
Sex	Female	75	52
	Male	70	48
Age group	≤ 30 years	46	29.9
	31-40 years	38	24.7
	41-50 years	32	20.8
	51-60 years	28	18.2
	> 60 years	10	6.5
Educational level	Basic	7	5
	High school	3	2
	High school	55	38
	Superior	72	50
	Fourth level	8	6

Note: Mean age: 40.75 ± 13.46 years (95% IC: 38.56-42.94)



The analysis of educational level revealed a significant concentration in higher education, with 72 patients (50%) at the higher level and 8 patients (6%) at the fourth level, representing 56% of the sample with university or postgraduate training. Baccalaureate was represented by 55 patients (38%), while secondary and basic education were in the minority with 3 (2%) and 7 (5%) patients, respectively (Table 1).

Assessment of Cognitive Decline Using BICAMS

The results of the cognitive assessment showed differentiated patterns between the three subtests. BVMTR had a mean score of 24.43 ± 9.30 (95% IC: 22.89-25.97), with 15 patients (10.3%) exhibiting CI. The CVLT-II showed a mean of 34.57 ± 12.65 (95% IC: 32.48-36.66), also with 15 patients (10.3%) with CI. The SDMT showed a mean of 29.17 ± 11.81 (95% IC: 27.22-31.12), but with only 9 patients (6.2%) reflecting CI (Table 2).

Table 2

Cognitive performance and cognitive impairment by BICAMS subtests

Test	Medium (SD)	IC 95%	No CI n (%)	With CI n (%)
BVMTR	24.43 (9.30)	22.89-25.97	130 (89.7)	15 (10.3)
CVLT-II	34.57 (12.65)	32.48-36.66	130 (89.7)	15 (10.3)
SDMT	29.17 (11.81)	27.22-31.12	136 (93.8)	9 (6.2)

Note: SD: standard deviation; IC: confidence interval; CI: cognitive impairment

Relationship between demographic factors and cognitive impairment

Age: A statistically significant association was found between age and CI as measured by BVMTR ($\chi^2=14.02$, $p=0.007$). The 31-40 and >60 age groups had a higher proportion of cases with CI. The SE was mean (0.35) with a statistical power of 62%, which indicates that the 80% was not reached, which would allow evidence of a real effect if it exists. This increases the risk of making a type II error (false negative) (Table 3).

Table 3

Inferential analysis of associations between demographic factors and cognitive impairment (χ^2 test)

Related variables	Value	p-value	Effect Size	Power (1-b)
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Related variables	Value	p-value	Effect Size	Power (1-b)
BVMTR and Age Groups	14.02	0.007*	0.35	0.62
BVMTR and Sex	0.46	0.498	-	-
BVMTR and Educational Level	36.82	<0.001**	0.67	0.84
CVLT-II and Age Groups	4.97	0.290	-	-
CVLT-II and Sex	0.17	0.679	-	-
CVLT-II and Educational Level	10.48	0.033*	0.77	0.96
SDMT and Age Groups	8.29	0.081	-	-
SDMT and Sex	1.30	0.254	-	-
SDMT and Education Level	0.494	0.293	-	-

*p<0.05; **p<0.001

Level of education: a highly significant association between educational level and CI was observed in BVMTR ($\chi^2=36.82$, $p<0.001$) and CVLT-II ($\chi^2=10.48$, $p=0.033$). For BVMTR, the effect size was medium-high ($d=0.67$) with statistical power of 84%. For CVLT-II, the SE was high ($d=0.77$) with a very good statistical power of 96% (Table 3).

Sex: no significant association was found between sex and cognitive impairment in any of the three tests ($p>0.05$ for all), indicating that there are no significant differences in the risk of CI between men and women in this sample (Table 3).

Contingency analysis by age groups

The detailed analysis by age group revealed that, for BVMTR, no patient ≤ 30 years old presented CI, while the 31-40 year old group showed the highest absolute frequency ($n=8$). For CVLT-II, the distribution was more homogeneous between groups, with greater involvement in the 41-50 age group ($n=6$). In the SDMT, a higher concentration of cases was observed in the 31-40 year old group ($n=6$) (Table 4).

Table 4

Distribution of cognitive impairment by age groups and BICAMS subtests

Subtest	Age group	No CI (n)	With CI (n)	Total (n)
BVMTR	≤ 30 years	37	0	37
	31-40 years	30	8	38
	41-50 years	30	2	32

Subtest	Age group	No CI (n)	With CI (n)	Total (n)
	51-60 years	26	2	28
	>60 years	7	3	10
CVLT-II	≤30 years	35	2	37
	31-40 years	35	3	38
	41-50 years	26	6	32
	51-60 years	26	2	28
	>60 years	8	2	10
SDMT	≤30 years	36	1	37
	31-40 years	32	6	38
	41-50 years	31	1	32
	51-60 years	27	1	28
	>60 years	10	0	10

CI: cognitive impairment

DISCUSSION

The findings provide relevant evidence on the relationship between demographic factors and CI in Ecuadorian patients with RRMS, contributing to scientific knowledge in a population traditionally underrepresented in the international literature.

Prevalence of cognitive impairment

The prevalence of cognitive impairment observed (6.2-10.3%) was notably lower than those reported in recent meta-analyses describing prevalences of 32.5-44% (3-4). This discrepancy can be explained by several factors. First, the high proportion of patients with higher education (56%) in the sample could confer greater cognitive reserve, acting as a protective factor against deterioration (10). Second, the specific characteristics of RRMS in Ecuadorian populations may differ from those observed in European and North American populations due to particular genetic, environmental, or lifestyle factors (12).

Demographic factors as predictors

Age: The significant association between age and CI, particularly in the visuospatial domain (BVMTR), is consistent with previous studies that identify age as a robust predictor of cognitive functioning in MS (9). The bimodal pattern observed, with greater involvement in groups of 31-40 years and >60 years, indicates the possible

presence of differentiated mechanisms. In the younger group, CI may reflect more aggressive forms of the disease, while in older patients it may represent the cumulative effect of aging and disease progression (16).

Educational level: The strong association between educational level and cognitive performance, particularly observed in BVMTR and CVLT-II, reinforces the concept of cognitive reserve as a protective factor (10). From the observed high effect sizes ($TE=0.67-0.77$), it can be deduced that education is a clinically relevant determinant of cognitive functioning in MS. The results are consistent with multicenter studies that support the protective role of higher education against CI (17).

Sex: The absence of an association between sex and CI contrasts with some studies that report differences based on sex (11). This absence of association could reflect specific characteristics of the Ecuadorian coastal population or methodological differences in the definition of CI. Recent work has indicated that gender differences in cognition may be more subtle and require more sophisticated analyses to detect (18).

Specific patterns by cognitive domain

The relative preservation of processing speed (SDMT: 6.2% of DI) contrasts with the literature that typically identifies this domain as the most vulnerable¹⁹. Such an observation could reflect particularities of the population studied or differences in the sensitivity of the test in specific cultural contexts. The greater involvement of memory domains (BVMTR and CVLT-II: 10.3% each) allows us to infer a pattern of deterioration that privileges the mnemonic systems over the attentional systems in this sample.

Clinical implications

The results suggest the need to develop cognitive assessment strategies that specifically consider the patient's educational level and age. The high proportion of patients with higher education in the sample raises questions about possible biases in accessing specialized services that require additional research (20).

Strengths and limitations

The study's strengths include the use of an internationally validated tool (BICAMS), comprehensive analysis of demographic factors, and focus on an underrepresented population. Limitations include (a) the cross-sectional design that prevents causal inferences from being considered, (b) the relatively small sample size for some subgroups, and (c) the possible presence of selection biases related to educational level.

Future prospects

The findings open up important lines of research, including longitudinal studies assessing the progression of CI, analysis of genetic and environmental factors specific to the Ecuadorian population in general, and the development of local standards for neuropsychological testing. There is also a need to investigate early intervention strategies based on the identified predictors.

CONCLUSIONS

Demographic factors, specifically age and level of education, were shown to be significant predictors of CI in Ecuadorian patients with RRMS. The absence of association with sex suggests that this factor is not a relevant determinant in the coastal population investigated.

The low prevalence of CI observed, in contrast to international studies, raises important questions about the specific characteristics of RRMS in Ecuador and the role of cognitive reserve as a protective factor. The high proportion of patients with higher education in the sample shows the need to investigate possible disparities in access to specialized services.

The results have immediate clinical implications for neurological practice, suggesting the implementation of cognitive assessment protocols that particularly consider the age and educational level of the patient. The findings open up prospects for the development of early intervention strategies aimed at higher-risk populations.

New research perspectives include: (1) longitudinal studies assessing the temporal evolution of cognitive impairment and its predictors; (2) research on genetic and environmental factors specific to the Ecuadorian population; (3) development of local

standards for neuropsychological testing that consider educational and cultural characteristics; (4) analysis of disparities in access to specialized services; and (5) design of culturally adapted cognitive rehabilitation interventions.

The evidence generated contributes to scientific knowledge about MS in Latin American populations and provides a solid basis for the development of public health policies aimed at improving early diagnosis, comprehensive evaluation, and optimized management of patients with MS in Ecuador.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this research.

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AUTHOR CONTRIBUTION

Conceptualization and design: R.E.C.E.; Methodology: V.M..R; Formal analysis: VMR; Research: R.E.C.E.; Deed - original draft: F.I.M.V.; Writing - revision and editing: V.M..R.; Supervision: V.M..R /M.G.A.C.

DATA AVAILABILITY

The data supporting the conclusions of this article are available upon reasoned request to the corresponding author, respecting the ethical and confidentiality considerations of the study.

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