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Brief Report

Cognitive impairment in patients with rheumatoid arthritis in relation to disease activity: A cross-sectional observational study

Deterioro cognitivo en pacientes con artritis reumatoide en relación con la actividad de su enfermedad: un estudio observacional de corte transversal

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is an immune-mediated disease that affects multiple organs. Among its extra-articular manifestations is cognitive impairment (CI).
Methodology: This was an observational, cross-sectional study with an analytical approach, including 59 patients with RA from three specialized outpatient centers in the city of Pasto, Colombia. Data were collected on disease activity using the DAS28 scale, as well as the degree of CI using the Montreal Cognitive Assessment (MoCA).
Results: A total of 44.1% of participants were classified as having suspected CI, with lower performance across all assessed subdomains. The most affected domains were visuospatial abilities and language. In the multivariate model, lower educational level was associated with CI, while age, glucocorticoid use, disease activity, and functional disability did not show an independent association.
Conclusion: CI has a higher prevalence in patients with RA compared with the general population, with no relationship found between CI and disease activity.

Palabras clave:
Artritis reumatoide
Deterioro cognitivo
Actividad de la enfermedad

RESUMEN

Introducción: La artritis reumatoide (AR) es una enfermedad inmunomediada que afecta múltiples órganos, dentro de las manifestaciones extraarticulares se encuentra el deterioro cognitivo (DC).
Metodología: Estudio observacional, de corte transversal con intención analítica en el cual participaron 59 pacientes con AR de tres centros de consulta especializada en la ciudad de Pasto, Colombia, de quienes se recolectó datos sobre la actividad de la enfermedad mediante la escala DAS28, así como el grado de DC mediante la evaluación cognitiva de Montreal (MoCA).
Resultados: El 44,1% fue clasificados como sospecha de DC, teniendo menor rendimiento en todos los subdominios evaluados, siendo los más afectados, visoespacial y lenguaje. En el modelo multivariado, el menor nivel educativo se asoció con DC, mientras que la edad, el uso de glucocorticoides, la actividad de la enfermedad y la discapacidad funcional no mostraron asociación independiente.
Conclusión: El DC tiene mayor prevalencia en pacientes con AR en comparación con la población en general, sin encontrar relación con actividad de la enfermedad.

Introduction

Rheumatoid arthritis (RA) is an immune-mediated inflammatory disease that predominantly affects the joints. It causes significant direct and indirect costs, determined by disability, losses in work productivity, and a decrease in quality of life.[1] It affects between .3% and 1.2% of the

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world's population, with a higher prevalence in women (2:3 ratio).[1,2] Due to its pathophysiology related to chronic systemic inflammation, it is associated with extra-articular manifestations, which affect approximately 40% of patients.[3] Among the most affected systems are the skin, respiratory, cardiovascular, and central nervous systems,[4] the latter being a relevant and understudied factor, with variable manifestations that include cognitive impairment (CI).

A cross-sectional study evaluated the prevalence of CI in patients with RA and found that they exhibit significantly lower performance on cognitive tests. Furthermore, it identified factors such as age, educational level, disease activity, and depression as associated variables. These findings suggest that cognitive impairment (CI) is highly prevalent in older adults with rheumatoid arthritis (RA) and appears to be related to increased inflammatory activity, supporting the hypothesis that chronic systemic inflammation could accelerate this process.[5]

Given the importance of cognitive function in daily life, it is essential to understand the biological and clinical factors that can influence it, as this will allow for the development of strategies and interventions to improve quality of life. The objective of this study was to investigate the prevalence of CI in a population with RA and to identify specific factors associated with its presence.

Materials and methods

This was an observational, cross-sectional study with an analytical purpose, conducted in three specialised outpatient clinics in the city of Pasto, Colombia, over a period of 6 months in 2024. Patients over 18 years of age with a diagnosis of seropositive RA were included, excluding those with a history of psychiatric illness and a prior diagnosis of mild CI or dementia. A non-probability convenience sampling method was used; participants voluntarily agreed to participate and provided their informed consent. Data collection involved a survey that included sociodemographic information, the DAS-28 clinimetric scale, which assesses disease activity based on clinical and laboratory variables,[6] the HAQ test, which provides a global assessment of quality of life and includes 20 items covering physical actions in eight domains: dressing and grooming, getting up, eating, walking, personal hygiene, reaching, grasping, and outdoor activities,[7] and the Latin American validated Spanish version of the MoCA test, which examines the following skills: attention, concentration, executive functions, memory, language, visuospatial skills, calculation, and orientation.[8]

Statistical analysis was performed using IBM Statistical Package for the Social Sciences software, licensed by the University of Nariño. Quantitative variables were described using measures of central tendency and dispersion. A bivariate analysis was conducted to identify potential factors associated with the presence of cognitive impairment (CI), with *P*-values $<.05$ considered positive. For qualitative variables, results were expressed as absolute and relative values. The chi-square test was used to identify associations between cognitive impairment (CI) and the independent variables, and crude and adjusted relative prevalences were determined in the final analysis model. The research was approved by the Curriculum and Research Committee of the Medicine Programme at the University of Nariño.

Results

A total of 59 patients were included. Sociodemographic and clinical characteristics are presented in Table 1. The mean age was 54.71 years (SD: 12.7), 83.1% were female, and 34.7% had >12 years of schooling. Clinical characteristics of RA were obtained from clinical records and were not fully available. The mean MoCA test score adjusted for education level was 24.08 (SD: 4.211), and the mean and standard deviation of the subdomains were: visuospatial, 3.80 ± 1.01 of 5; identification, 2.81 ± 0.39 of 3; attention, 4.32 ± 1.42 of 6; language, 2.2 ± 0.84 of 3; Abstraction: 1.75 ± 0.54 out of 2; memory: 2.61 ± 1.59 out of 5; and

Table 1
Clinical and sociodemographic variables.

Sociodemographic variables		
Age	Under 60	36 (61%)
	Over 60	23 (39%)
Sex	Woman	49 (83.1%)
	Man	10 (16.9%)
Socioeconomic level	Strata 1	33 (55.9%)
	Strata 2	19 (32.2%)
	Strata 3	6 (10.2%)
	Strata 4	1 (1.7%)
Schooling	Incomplete primary	24 (40.7%)
	Complete primary	11 (18.6%)
	Incomplete secondary	5 (8.5%)
	Complete secondary	13 (22.0%)
	Higher education	6 (10.2%)
Origin	Urban area	34 (57.6%)
	Rural area	25 (42.4%)
Ethnic origin	Mestizo	53 (89.8%)
	Indigenous	5 (8.5%)
	Afro-descendant	1 (1.7%)
Affiliation	Subsidised	45 (76.3%)
	Contributory	14 (23.7%)
Occupation	Homemaker	23 (39.0%)
	Sales people and vendors	10 (16.9%)
	Agriculture and farm work	7 (11.9%)
	Health and education	5 (8.5%)
	Unemployed and pensioners	2 (3.4%)
	Others	12 (20.3%)
Pharmacological management with DMARDs	Methotrexate	32 (54.2%)
	Leflunomide	31 (52.5%)
	Hydroxychloroquine	11 (18.6%)
	Chloroquine	8 (13.6%)
	Azathioprine	2 (3.4%)
	Sulfasalazine	2 (3.4%)
Pharmacological management with biologics	Abatacept	8 (13.6%)
	Anti TNF	6 (10.2%)
	JAK inhibitor	6 (10.2%)
	Rituximab	1 (1.7%)
Pain management	Use of glucocorticoids	28 (47.5%)
	Use of NSAIDS	25 (42.4%)
Background	Hypertension	17 (28.8%)
	Dyslipidaemia	11 (18.6%)
	Depression	11 (18.6%)
	Smoking	9 (15.3%)
	Obesity	9 (15.3%)
	Anaemia	6 (10.2%)
	Other rheumatic disease	6 (10.2%)
	Diabetes Mellitus	4 (6.8%)
	Alcoholism	3 (5.1%)
	Heart disease	2 (3.4%)
	Stroke	1 (1.7%)
Clinical variables		
Length of time with the disease	Under 5 years	11 (18.6%)
	Between 5 and 10 years	17 (28.8%)
	Over 10 years	31 (52.5%)
Disease activity	Remission	17 (29.8%)
	Mild activity	12 (21.1%)
	Moderate activity	23 (40.4%)
	Severe activity	5 (8.8%)
HAQ	No disability	32 (54.2%)
	Mild disability	15 (25.4%)
	Moderate	11 (18.6%)
	Maximum disability	1 (1.7%)

Table 1 (*Continued*)

Positive PCR (n = 32)		21 (65.6%)
Positive ESR (n = 57)		32 (56.1%)
Positive anti-CCP (n = 29)		29 (100.0%)
Positive RF (n = 41)		40 (97.6%)
Suspected cognitive impairment	Yes	26 (44.1%)
	No	33 (55.9%)

Anti-TNF: anti-tumour necrosis factor; Anti-CCP positive > 17 IU/ml; Anti-CCP: anti-cyclic citrullinated peptide antibodies; CRP positive > 1 mg/dl; CRP: C-reactive protein; DMARDs: disease-modifying anti-rheumatic drugs; ESR positive in women > 20 mm/h in men > 15 mm/h; ESR: erythrocyte sedimentation rate; JAK inhibitor: Janus kinase inhibitor; NHAQ: Health Assessment Questionnaire; NSAIDs: non-steroidal anti-inflammatory drugs; RF positive > 16 IU/ml; RF: rheumatoid factor.

orientation: 5.81 ± 0.47 out of 6. The proportion of participants classified as having suspected DC according to a cutoff score <25/30 was 44.1%.

The statistically significant association between suspected DC, as measured by the MoCA test, and the study variables is presented in Tables 2 and 3. Bivariate analysis revealed associations with sociodemographic, clinical, and treatment-related variables.

Subsequently, in the multivariate model, given the sample size, variables with clinical plausibility and potential confounding on MoCA performance were selected. The adjusted model included age over 60 years, educational level, glucocorticoid use, disease activity, and the HAQ test. After adjustment, a higher level of education emerged as a protective factor, while the remaining variables did not show an independent association (Table 3).

Discussion

This study presents a limited sample of patients, in which a prevalence of suspected cognitive impairment (CI) of 44.1% was obtained using a cutoff point <25/30 of the Spanish version of the MoCA. Previous studies using the same tool, such as that by Katchamart et al.[9] reported a prevalence of 70%. McDowell et al., for their part, found a prevalence of 72.2% with a cutoff point <27/305. The most affected subdomains are consistent with previous reports, with language, visuospatial skills, and memory being the most impaired areas. Physiological studies have shown that these findings are related to hypoperfusion in the parietal and frontal lobes, evidenced by magnetic resonance imaging and positron emission tomography.[10]

Regarding disease activity, the bivariate analysis showed an association between DAS28 categories and suspected brain damage, particularly in the moderate activity group. However, this relationship was not consistently maintained in the multivariate model, which differs from studies indicating that a DAS28 score > 2.6 is associated with a higher risk (RR = 2.23 [1.07–4.37]) and with adjusted RRs of 1.10 and 1.43 for moderate and severe activity, respectively.[5,9] One possible explanation is the sample size; however, other studies indicate that brain damage is more related to the permeability of the blood-brain barrier than to serum levels of circulating antibodies, suggesting a multifactorial process that may differ among populations.[11]

In the bivariate analysis, associations were also observed between suspected cognitive impairment (CI) and variables such as female sex, age over 60 years, use of glucocorticoids, methotrexate, and sulfasalazine, as well as with the degree of functional disability measured by the HAQ test. However, these associations did not remain independent in the multivariate model.

Furthermore, educational level showed an independent association with suspected CI in the multivariate model. This finding is consistent with the existing literature, where educational level has been described as one of the main determinants of performance on cognitive scree-

Table 2
Factors associated with cognitive impairment: bivariate analysis.

Variable	Mild cognitive impairment		*P*
	Yes	No	
Sex			
Feminine	19 (38.8)	30 (61.2)	.040
Masculine	7/70.0)	3 (30.0)	
Over 60 years			
Yes	14 (53.8)	9 (27.3)	.030
No	12 (46.4)	24 (72.7)	
Socioeconomic level			
Strata 1	19 (57.6)	14 (42.4)	
Strata 2	5 (26.3)	14 (73.7)	
Strata 3	2 (33.3)	4 (66.7)	.279
Strata 4	0 (0)	1 (100)	<.01
Schooling			
Incomplete primary	18 (75)	6 (25)	
Complete primary	5 (45.5)	6 (54.5)	.108
Incomplete secondary	0 (0)	5 (100)	<.001
Complete secondary	3 (23.1)	10 (76.9)	.001
University	0 (0)	6 (100)	<.001
Origin			
Urban	10 (29.4)	24 (70.6)	.005
Rural	16 (64)	9 (36)	
Ethnic origin			
Afro-descendant	1 (100)	0 (0.0)	<.01
Indigenous	1 (20)	4 (80)	.221
Mestizo	24 (45.3)	29 (54.7)	
Occupation			
Agriculture and farm work	4 (57.1)	3 (42.9)	.295
Homemaker	12 (52.2)	11 (47.8)	**.282**
Salespeople and vendors	5 (50)	5 (50)	.422
Unemployed and pensioners	1 (50)	1 (50)	.647
Health and education	0 (0)	5 (100)	.005
Others	4 (33.3)	8 (66.7)	
Methotrexate consumption			
Yes	19 (59.4)	13 (40.6)	.006
No	7 (25.9)	20 (74.1)	
Sulfasalazine consumption			
Yes	0 (0)	2 (100)	< .001
No	26 (45.6)	31 (54.4)	
Use of Anti TNF			
Yes	0 (0)	6 (100)	<.001
No	26 (49.1)	27 (50.9)	
Use of glucocorticoids			
Yes	9 (29)	22 (71)	.010
No	17 (60.7)	11 (39.3)	
Anaemia			
Yes	5 (83.3)	1 (16.7)	.005
No	21 (39.6)	32 (60.4)	
Alcoholism			
Yes	3 (100)	0 (0.0)	<.001
No	23 (41.1)	33 (58.9)	
Duration of the disease			
Under 5 years	2 (18.2)	9 (81.8)	.049
Between 5 and10 years	9 (52.9)	8 (47.1)	0.762
Over 10 years	15 (48.4)	16 (51.6)	
Disease activity			
Remission	5 (29.4)	12 (70.6)	.660
Mild activity	4 (33.3)	8 (66.7)	.560
Moderate activity	15 (65.2)	8 (34.8)	.047
Severe activity	1 (20)	4 (80)	
HAQ			
No disability	11 (34.4)	21 (65.6)	.025
Mild disability	10 (66.7)	5 (33.3)	.905

Table 2
(*Continued*)

Variable	Mild cognitive impairment		*P*
	Yes	No	
Moderate disability	4 (36.4)	7 (63.6)	<.001
Maximum disability	1 (100)	0 (0)	

Anti-TNF: anti-tumour necrosis factor; HAQ: Health Assessment Questionnaire.

Table 3
Factors associated with cognitive impairment: multivariate analysis.

Variable	Prevalence ratio Crude PR (95% CI)	Prevalence ratio Adjusted PR (95% CI)
Over 60 years		
Yes	1.21 (1.018–1.429)	1.13 (.989–1.308)
No	1	1
Use of glucocorticoids		
Yes	1.25 (1.054–1.472)	1.10 (.919–1.318)
No	1	1
Disease activity		
Remission	1	1
Mild activity	1.04 (.794–1.337)	1.05 (0.840–1.308)
Moderate activity	1.28 (1.040–1.567)	1.16 (0.929–1.444)
Severe activity	.93 (.662–1.298)	1.03 (.754–1.421)
Test HAQ		
No disability	1	1
Mild disability	1.23 (1.018–1.487)	1.08 (0.885–1.329)
Moderate disability	.96 (.746–1.234)	.84 (.654–1.079)
Severe disability	1.48 (1.304–1.672)	.99 (.833–1.197)
Schooling		
Incomplete primary	1	1
Complete primary	.86 (.685–1.087)	.95 (.738–1.225)
Incomplete secondary	.57 (.519–.638)	.64 (.527–.782)
Complete secondary	.71 (.572–.875)	.80 (.646–1.002)
University	.57 (.519–.638)	.60 (.516–.710)

HAQ: Health Assessment Questionnaire.

ning tests. It has been proposed that higher levels of education could confer greater cognitive reserve, allowing for compensation or delay of the clinical manifestation of cognitive impairment.[12]

In previous studies, some variables associated with suspected CI included female sex as a protective factor (PR = .74; 95% CI: .03–1.45) in the study by McDowell et al.[5] In contrast, increasing age is associated with a higher risk of dementia, probably due to immunosenescence, a process involving decreased T-cell function and increased susceptibility to inflammatory processes, thus favouring dementia.[13]

Prolonged glucocorticoid use is associated with decreased neurotrophic factors, neuronal death, hippocampal atrophy, and dendrite loss.[14] Methotrexate use was associated with a lower risk of dementia (OR = .71; 95% CI: .52–.98).[15] Finally, although our study did not identify a relationship between functional limitation as measured by the HAQ, some studies show a negative correlation with MoCA scores (r = –.27; $P < .001$).[16]

Conclusion

This study had limitations related to sample size; However, it provides relevant information by confirming a high prevalence of dementia in patients with rheumatoid arthritis (RA) and identifying associated factors such as female sex, advanced age, low socioeconomic and educational level, and the use of certain medications. Although disease activity did not show a direct relationship with dementia, longer disease duration and disability do increase the risk. These findings highlight the importance of physicians identifying these risk factors early in order to offer timely interventions that mitigate the impact of dementia on patients' quality of life.

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Declaration of competing interest

The authors have no conflict of interest to declare with this research.

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