Original Article

Prevalence of Cognitive Impairment among Iraqi Patients with Ankylosing Spondylitis

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Abstract

Background: Ankylosing spondylitis (AS) is the prototype of spondyloarthropathies and one of the common rheumatic diseases (RDs). Various degrees of cognitive impairment have been reported with most autoimmune RDs. **Objectives:** To estimate the prevalence of cognitive impairment in AS patients and its relationship to disease activity and functional limitations and the effect of various sociodemographic and clinical characteristics on cognitive function in AS patients. **Materials and Methods:** This case–control study comprised 100 patients with AS and 100 healthy subjects who were matched for age, gender, and educational level. Private interviews were conducted with participants to complete the questionnaire and evaluate cognitive function using the 6-item Cognitive Impairment Test (6-CIT) and the Montreal Cognitive Assessment (MoCA). **Results:** According to MoCA, 48% of AS patients and 16% of healthy controls were cognitively impaired ($P = 0.001$). By 6-CIT, 6% of the AS group had cognitive impairment, whereas all 100 controls had normal cognitive function ($P = 0.029$). There was a significant direct correlation between 6-CIT score with marital status ($P = 0.020$), BMI ($P = 0.021$), and Bath Ankylosing Spondylitis Disease Activity Index ($P = 0.008$) and inverse correlation with employment ($P = 0.015$), education ($P = 0.008$), and family income ($P = 0.12$). There was significant direct correlation between MoCA with employment ($P = 0.009$), education ($P = 0.005$), family income ($P = 0.022$), and use of non-steroidal anti-inflammatory drugs (NSAIDs) ($P = 0.008$) and inverse correlation with marital status ($P = 0.002$). **Conclusions:** Patients with AS have a higher degree of cognitive impairment than healthy individuals. It is associated with disease activity, lower socioeconomic status, being widowed, and obesity. Use of NSAIDs is associated with lower cognitive impairment.

Keywords: Ankylosing spondylitis, cognitive function, cognitive impairment, rheumatic diseases

Introduction

Ankylosing spondylitis (AS) is the prototype of spondyloarthropathies and one of the common rheumatic diseases (RDs). Sacroiliitis is the earliest recognized manifestation of AS, but peripheral joints and extra-articular structures may also be affected.[1] It can affect the quality of life, morbidity, mortality, participation in paid and unpaid work, and healthcare costs.[2] Extra-articular manifestations vary widely in terms of both frequency and severity.[3] AS has been linked to a variety of neurological complications, including spinal cord or nerve compression due to atlantoaxial subluxation or vertebral fractures, cauda equine syndrome, and transverse myelitis.[4] When compared to clinically manifest complications, subclinical neurological complications are more common in AS.[5]

For patients with chronic diseases including RDs, intact cognitive function is critical for daily functioning, treatment compliance, and self-management.[6] Various degrees of cognitive impairment have been reported with most autoimmune RDs.[7] One study showed that 49.0% of patients with RDs have cognitive impairment, which is comparable to the reported incidence rates of 40%–70% for cognitive impairment following stroke.[8] Approximately 23.6% of AS patients self-reported concepts related to

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cognitive impairment.[9] Cognitive impairment might be overlooked in AS.

The purpose of this study was to determine the prevalence of cognitive impairment among patients with AS and its relationship to disease activity and functional limitations and to evaluate the effect of various sociodemographic and clinical characteristics on cognitive function in AS patients.

Materials and Methods

Study design

This observational case–control study was undertaken at the Rheumatology Unit in a tertiary hospital from December 2020 to August 2021 (research was authorized on January 26, 2021, no. 363).

Subjects

Patients with AS were recruited consecutively when they attend the Rheumatology Consultant Clinic. Adults with AS diagnosed using the Modified New York criteria for the diagnosis of AS were considered eligible for the study. The study included 100 healthy subjects who have been matched to the patients in terms of age, gender, and educational level. Patients with any of the following conditions were precluded from the study: less than 18 years of age, overlap with other autoimmune RDs, acute or chronic infection, previous or current diagnosed underlying malignancy, underlying chronic medical illnesses known to affect cognitive function such as hypothyroidism and stroke, and primary psychiatric disorders such as depression.

Data collections

Data were collected through private interviews with the participants to complete the questionnaire that was organized before the interview as well as cognitive function testing. The interview lasted approximately 30 min. Data collected include:

1. Sociodemographic characteristics: age, gender, address, education, occupation, marital status, smoking, alcohol intake, monthly family income, and body mass index (BMI).
2. Clinical characteristics: comorbidities such as hypertension (HT), diabetes mellitus (DM) and hyperlipidemia, cardiovascular diseases, and previously diagnosed neurological or psychiatric diseases.
3. Disease characteristics: disease duration, medications used, and erythrocyte sedimentation rate (ESR). The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to determine disease activity. The Bath Ankylosing Spondylitis Functional Index (BASFI) was implemented to evaluate functional ability.

Cognitive function of participants was assessed by 6-item cognitive impairment test (6-CIT) Kingshill Version 2000, and Montreal Cognitive Assessment (MoCA) test. 6-CIT is recommended as a cognitive screening tool and it consists of three temporal orientation tests, two attention tests, and a short-term memory test. It is graded out of 28 points, with a 7/8 cut-off (8 is abnormal).[10] Arabic version of 6-CIT had been used after performing a pilot study to assess its face validity. Where it was translated forward to Arabic by a language expert, with additional notes from professional physicians, and then translated back to English by a language expert. Following that, it was given to 10 patients with AS to assess their perception and understanding of its items. Montreal cognitive assessment is 30 points screening test that is conducted in 10–12 min to detect cognitive impairment. Using 10 subtests, it can assess visuospatial and executive skills, naming, attention, language, abstraction, delayed recall, and orientation to time and place. Cognitive impairment is indicated with a score of less than 26. An extra point is added if the individual has 12 years or fewer of formal education.[11] Arabic version was already available and validated for use.[12] For participants who are illiterate or with less than 5 years of education. Arabic version of MoCA-basic was used to assess their cognitive function.

Statistical analysis

The data were analyzed using International Business Machines (IBM) Corporation, Statistical Package for Social Sciences (SPSS), version 25 (IBM Corp., Armonk, New York, USA). Chi-square test was used to assess the association between different categorial variables, whereas Fisher exact test was utilized with a predicted frequency of less than 5. Bivariate correlation analysis was applied to describe the relationship between cognitive impairment and sociodemographic and clinical predictors. Pearson's correlation test was used to investigate the relationship between continuous variables. Spearman's correlation test was used to investigate the relationship between categorical variables. The correlation coefficient value ranged between zero to one and the value of the coefficient closer to one indicates a stronger correlation. The sign of the coefficient describes the direction of the correlation between the two variables where a negative sign indicates inverse correlation while no sign indicates direct correlation. Then multiple linear regression analysis was done to detect the impact of various independent variables on the cognitive impairment scores using dummy variables. A probability value (P value) < 0.05 was considered statistically significant.

Ethical approval

This study was carried out in accordance with the Helsinki Declaration's ethical principles. The institutional ethics committee of the University of Karbala approved the study under the reference No. 33 on April 13, 2020, and all ethical and privacy standards (local, national and international) were followed.

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Results

Sociodemographic and baseline characteristics

The total number of participants in the current study was 200, in that 100 had confirmed AS, and 100 healthy subjects. Each group comprised 77 male participants and 23 female participants. The mean age of AS patients was 39.1 ± 8.8, ranging from 18 to 56 years whereas the mean age of the control group was 37.9 ± 9.6 years, ranging from 18 to 55 years. There was no significant difference between AS patients and controls in terms of age, gender, address, marital status, occupation, educational level, monthly family income, BMI, smoking, and alcohol intake [Table 1]. Median disease duration was five years. Sixty-four percent of patients had inactive disease, 60% had no functional limitations, 60% had current or previous long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs), and 86% were using tumor necrosis factor inhibitor (TNFi). Sixty-eight percent of AS patients have no comorbidities.

Cognitive function

Comparing AS patients to healthy individuals, cognitive impairment was statistically significantly higher in AS patients. According to MoCA test, 48% of AS patients were cognitively impaired compared to 16% of healthy controls (P = 0.001). By 6-CIT assessment, cognitive impairment was recorded among 6% in the AS group, whereas all 100 healthy controls had normal cognitive function (P = 0.029) [Table 2]. In terms of individual cognitive domains, individuals with AS performed considerably worse than controls in visuospatial/executive skills, language, attention, abstraction, and orientation ($P \leq 0.05$).

Association between cognitive impairment and ankylosing spondylitis patients' sociodemographic and clinical characteristics

The 6-CIT score had a significant direct correlation with marital status, BMI, and BASDAI. Furthermore, there is a significant inverse correlation with employment, education, and family income. In multiple regression analysis, marital status, BASDAI, and NSAIDs were significant predictors of cognitive impairment. R square = 0.35. As illustrated in Table 3.

There was a significant direct correlation between MoCA score with employment, education, family income, and NSAIDs. And significant inverse correlation with marital status. In multiple regression analysis, marital status and NSAIDs were significant predictors of cognitive impairment. R square = 0.37. As illustrated in Table 4.

Table 1: Comparison between study groups by certain sociodemographic and baseline characteristics

Demographic and baseline characteristics	Study groups		Total (%) n = 200	P value
	AS group (%) n = 100	Control group (%) n = 100		
Age (years), mean ± SD	39.13 ± 8.88	37.9 ± 9.6		0.348
Male	77 (77.0)	77 (77.0)	154(77.0)	0.998
Urban	90 (90.0)	94 (94.0)	184(92.0)	0.297
Employed	55 (55.0)	57 (57.0)	112(56.0)	0.776
BMI (kg/m^2), mean ± SD	29 ± 6.01	27.8 ± 4.47		0.100
Marital status				
Single	15 (15.0)	18 (18.0)	33(16.5)	0.453
Married	79 (79.0)	80 (80.0)	159(79.5)	
Divorced	4 (4.0)	2 (2.0)	6(3.0)	
Widowed	2 (2.0)	0 (0)	2(1.0)	
Education (schooling years)				
≤4	14 (14.0)	16(16.0)	30(15.0)	0.687
5–9	19 (19.0)	13 (13.0)	32(16.0)	
10–12	34 (34.0)	38 (38.0)	72(36.0)	
>12	33(33.0)	33 (33.0)	66(33.0)	
Family Income (ID)				
<500,000	37 (37.0)	24 (24.0)	61(30.5)	0.064
500,000–999,000	29 (29.0)	43 (43.0)	72(36.0)	
≥1,000,000	34 (34.0)	33 (33.0)	67(33.5)	
Smoking				
Non-smoker	50 (50.0)	62 (62.0)	112 (56.0)	0.204
Current smoker	40 (40.0)	32 (32.0)	72 (36.0)	
Ex-smoker	10 (10.0)	6 (6.0)	16 (8.0)	
Alcohol intake	2 (2.0)	3 (3.0)	5 (2.5)	0.651

AS: ankylosing spondylitis, n: number, P value: probability value, SD: standard deviation, ID: Iraqi dinars, BMI: body mass index (kg/m^2)

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Table 2: Comparison of MoCA and 6-CIT tests between the study groups

	AS group (%) $n = 100$	Control group (%) $n = 100$	*P* value
MoCA			
Impaired	48 (48.0)	16 (16.0)	0.001
Normal	52 (52.0)	84 (84.0)	
6-CIT			
Impaired	6 (6.0)	0 (0)	0.029
Normal	94 (94.0)	100 (100.0)	

AS: ankylosing spondylitis, *n*: number, *P* value: probability value, MoCA: Montreal cognitive assessment, 6-CIT: 6 item cognitive impairment test

Table 3: Results of bivariate correlation and multiple regression analysis of 6-item cognitive impairment test score with various variables of ankylosing spondylitis patients

Characteristic	6-CIT score			
	Bivariate correlation		Multiple linear regression	
	Correlation coefficient	*P* value	Beta coefficient	*P*-value
Age	0.107	0.289		
Gender	0.127	0.208		
Address	–0.011	0.915		
BMI	0.231	0.021	0.172	0.070
Marital status	0.219	0.020	0.371	0.000
Employment	–0.244	0.015	–0.036	0.763
Education	–0.263	0.008	–0.227	0.176
Family income	–0.250	0.012	–0.197	0.123
DM	0.088	0.386		
HT	–0.019	0.853		
Hyperlipidemia	0.121	0.231		
Smoking	–0.029	0.772		
Alcohol intake	0.024	0.810		
Disease duration	–0.026	0.795		
BASDAI	0.263	0.008	0.232	0.017
ESR	0.081	0.424		
BASFI	0.116	0.249		
NSAIDS	–0.176	0.081	–0.277	0.004
Glucocorticoids	0.081	0.424		
CsDMARD	0.181	0.072		
TNFi	–0.058	0.568		

6-CIT: 6-item cognitive impairment test, *P* value: probability value, BMI: body mass index, DM: diabetes mellitus, HT: hypertension, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, ESR: erythrocyte sedimentation rate, NSAIDs: non-steroidal anti-inflammatory drugs, CsDMARDs: conventional synthetic disease modifying anti-rheumatic drugs, TNFi: tumor necrosis factor inhibitor

Discussion

The current study showed a significantly increased frequency of cognitive impairment among AS patients compared with healthy individuals where 48% of patients had impaired performance using MoCA test and 6% of patients using 6-CIT. This is in line with a study by Vitturi *et al*.[13] in which AS patients had a considerably greater prevalence of subjects who were classified as cognitively impaired by MoCA (90.0% vs. 57.5%) than healthy individuals. Li *et al*.[14] was the first study to explore cortical activity changes related to AS utilizing resting-state functional magnetic resonance imaging (MRI) and revealed that patients with AS exhibited significantly reduced activity in the left medial frontal gyrus which is crucial for executive mechanisms, right precentral gyrus which is the primary motor cortex, and the right posterior cingulate cortex, which is implicated in integrating autobiographical, self-monitoring and social cognitive activities. Furthermore, increased activity in the left cerebellum anterior lobe can lead to affective, cognition, and movement regulation dysfunction. The altered spontaneous activity in the involved areas may represent possible characteristics of neurological impairment.

Cognitive impairment was associated with lower education and monthly family income. This result is in line with Sattler *et al*.[15] study which reported that high education was linked to an 85% reduced risk of mild cognitive impairment and Alzheimer's disease (AD)

Table 4: Results of bivariate correlation and multiple regression analysis of Montreal cognitive assessment score with various variables of ankylosing spondylitis patients

Characteristic	MoCA score			
	Bivariate correlation		Multiple linear regression	
	Correlation coefficient	*P* value	Beta coefficient	*P* value
Age	0.100	0.321		
Gender	–0.124	0.220		
Address	0.002	0.983		
BMI	–0.100	0.323		
Marital status	–0.312	0.002	–0.447	0.000
Employment	0.259	0.009	0.153	0.190
Education	0.279	0.005	0.082	0.610
Family income	0.228	0.022	0.205	0.098
DM	0.182	0.070		
HT	0.036	0.719		
Hyperlipidemia	0.025	0.803		
Smoking	0.088	0.382		
Alcohol intake	–0.007	0.941		
Disease duration	0.192	0.056		
BASDAI	0.138	0.105		
ESR	–0.032	0.754		
BASFI	0.102	0.314		
NSAIDS	0.265	0.008	0.252	0.005
Glucocorticoids	0.113	0.261		
CsDMARD	0.029	0.771		
TNFi	0.002	0.988		

MoCA: Montreal Cognitive Assessment, *P* value: probability value, BMI: body mass index, DM: diabetes mellitus, HT: hypertension, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, ESR: erythrocyte sedimentation rate, NSAIDs: non-steroidal anti-inflammatory drugs, CsDMARDs: conventional synthetic disease modifying anti-rheumatic drugs, TNFi: tumor necrosis factor inhibitor

compared to low education, and a high monthly household income was linked to a 69% lower risk of developing of both conditions. There was an inverse association between employment and cognitive dysfunction. Consistently Vance *et al*.[16] mentioned that engaging in stimulating and cognitively demanding activities can enhance cognition and cognitive reserve. Activities related to employment can have similar outcomes, and employment supports cognitive reserve through a variety of mechanisms, including the acquisition of new skills, social interactions, structured routine, purpose/meaning, and secured income.

There was a direct association between marital status and cognitive impairment. Similarly, Sun *et al*.[17] showed that unmarried older people were at a greater risk of cognitive dysfunction than married older people, and maintaining marriage in old age is more beneficial to cognition than being widowed, demonstrating the importance of robust and stable interpersonal relationships among older people.

Cognitive impairment was higher among patients with active disease and with obesity. This is in line with Mo *et al*.[18] study about the relationship of cognitive dysfunction with multi-dimension correlates of RD which revealed that disease activity had the strongest association with cognitive dysfunction among disease-related factors, and obesity appeared to have a significant direct association with cognitive dysfunction among health risk factors.

There was no association between cognitive impairment and comorbidities including DM, HT, and hyperlipidemia. Jang *et al*.[19] demonstrated that patients with AS had a higher prevalence of overall dementia and AD and despite the increased frequency of cardiovascular problems among AS patients, there was no increased prevalence of vascular dementia, and suggested that not having DM or HT was a risk factor for dementia.

Except for NSAIDs, which were associated with a lower risk of impaired cognitive performance, there was no significant association between the medications used by AS patients in the current study and cognitive impairment. This is in line with Wang *et al*.[20] study to explore the association between anti-inflammatory drugs and the incidence of AD, which showed that NSAID use resulted in a 28% lower risk of incident AD. Long-term use provides a greater benefit than short-term use (64% reduction). The blockage of cyclooxygenase-2 in the brain, which is significantly

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upregulated in affected areas of AD brain, may directly affect Aβ production by limiting microglial activation, or by activating peroxisomal proliferators-activated receptors, which inhibit the transcription of pro-inflammatory genes such as TNF-α, IL-6, cyclooxygenase-2, and cytokines. The main mechanism posited for cognitive impairment in RD is that RDs represent a state of chronic systemic inflammation with neurological involvement combined with accelerated atherosclerosis and autoantibodies. Studies also showed increased levels of pro-inflammatory cytokines in AD and related dementia.[21,22] It had been suggested that controlling systemic inflammation would decrease cognitive impairment risk among RD patients.

This is the first study to assess cognitive impairment among Iraqi patients with AS and a few studies worldwide. The current study has some limitations, such as a relatively small sample size due to collecting data over a short period and multiple exclusion criteria. There was no functional brain MRI to assess and map the brain activity associated with cognitive impairment in AS patients.

Conclusions

AS patients have a higher degree of cognitive impairment compared with healthy individuals. Cognitive impairment was associated with disease activity but not with functional limitations among AS patients. Also, it is associated with lower socioeconomic status, being widowed, and obesity. NSAID use is associated with reduced cognitive impairment. Larger longitudinal studies are required to confirm the results of this study and to search for other factors involved in the pathophysiology of cognitive impairment in patients with AS.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Sieper J, Braun J, Rudwaleit M, Boonen A, Zink A. Ankylosing spondylitis: An overview. Ann Rheum Dis 2002;61:iii8-18.
2. Boonen A, van der Linden SM. The burden of ankylosing spondylitis. J Rheumatol Suppl 2006;78:4-11.
3. El Maghraoui A. Extra-articular manifestations of ankylosing spondylitis: Prevalence, characteristics, and therapeutic implications. Eur J Intern Med 2011;22:554-60.
4. Mercieca C, van der Horst-Bruinsma IE, Borg AA. Pulmonary, renal and neurological comorbidities in patients with ankylosing spondylitis; implications for clinical practice. Curr Rheumatol Rep 2014;16:434.
5. Khedr EM, Rashad SM, Hamed SA, El-Zharaa F, Abdalla AK. Neurological complications of ankylosing spondylitis: Neurophysiological assessment. Rheumatol Int 2009;29:1031-40.
6. Shin SY. Factors influencing cognitive dysfunction in Korean patients with rheumatoid arthritis. J Korean Gerontol Nurs 2020;22:197-204.
7. Oláh C, Schwartz N, Denton C, Kardos Z, Putterman C, Szekanecz Z. Cognitive dysfunction in autoimmune rheumatic diseases. Arthritis Res Ther 2020;22:1-7.
8. Park J, Park W, Kwon S, Ham O, Suh Y, Jeong H, *et al*. Causal relationships between modifiable risk factors of cognitive impairment, cognitive function, self-management, and quality of life in patients with rheumatic diseases. Orthop Nurs 2018;37:305-15.
9. Sunkureddi P, Gibson D, Doogan S, Heid J, Benosman S, Park Y. Using self-reported patient experiences to understand patient burden: Learnings from digital patient communities in ankylosing spondylitis. Adv Ther 2018;35:424-37.
10. O'Sullivan D, O'Regan NA, Timmons S. Validity and reliability of the 6-item cognitive impairment test for screening cognitive impairment: A review. Dement Geriatr Cogn Disord 2016;42:42-9.
11. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, *et al*. The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53:695-9.
12. Abdel Rahman TT, El Gaafary MM. Montreal Cognitive Assessment Arabic version: Reliability and validity prevalence of mild cognitive impairment among elderly attending geriatric clubs in Cairo. Geriatr Gerontol Int 2009;9:54-61.
13. Vitturi BK, Suriano ES, Pereira de Sousa AB, Torigoe DY. Cognitive impairment in patients with ankylosing spondylitis. Can J Neurol Sci 2020;47:219-25.
14. Li C, Wei X, Zou Q, Zhang Y, Yin X, Zhao J, *et al*. Cerebral functional deficits in patients with ankylosing spondylitis—An fMRI study. Brain Imag Behav 2017;11:936-42.
15. Sattler C, Toro P, Schönknecht P, Schröder J. Cognitive activity, education and socioeconomic status as preventive factors for mild cognitive impairment and Alzheimer's disease. Psychiatry Res 2012;196:90-5.
16. Vance DE, Bail J, Enah CC, Palmer JJ, Hoenig AK. The impact of employment on cognition and cognitive reserve: Implications across diseases and aging. Nursing: Res Rev 2016;6:61-71.
17. Sun N, Jia R, Guo C, Sun T, Dong X, Li L, *et al*. Synergistic influence of education and marriage on the risk for cognition loss among older people in China. Nurs Open 2021;8:2616-21.
18. Mo J, Park J, Oh H. Correlates of cognitive impairment of rheumatic disease: Systematic review and meta-analysis. J Korean Acad Nurs 2016;46:1-18.
19. Jang HD, Park JS, Kim DW, Shin BJ, Lee JC, Choi SW, *et al*. Relationship between dementia and ankylosing spondylitis: A nationwide, population-based, retrospective longitudinal cohort study. PLoS ONE 2019;14:e0210335.
20. Wang J, Tan L, Wang HF, Tan CC, Meng XF, Wang C, *et al*. Anti-inflammatory drugs and risk of Alzheimer's disease: An updated systematic review and meta-analysis. J Alzheimer's Dis 2015;44:385-96.
21. Sood A, Raji MA. Cognitive impairment in elderly patients with rheumatic disease and the effect of disease-modifying anti-rheumatic drugs. Clin Rheumatol 2021;40:1221-31.
22. Al-Shaibani SAR, Jassim NA, Al-Bayati AAK. Raised inflammatory markers as predictors of response to anti-tumor necrosis factor drugs (etanercept and infliximab) in a sample of Iraqi patients with ankylosing spondylitis. Med J Babylon 2021;18:1241-4.