Evaluation of Severe Fatigue and Related Factors in Ankylosing Spondylitis: a Cross-Sectional Study

Ankilozan Spondilitte Şiddetli Yorgunluk ve İlişkili Faktörlerin Değerlendirilmesi: Kesitsel Bir Çalışma

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Abstract

Aim: Fatigue is an important symptom for patients with Ankylosing Spondylitis (AS). There is no accepted definitive scale to assess fatigue in AS. The purpose of the study was to measure fatigue by way of different scales in AS and find variables related to fatigue.

Method: The 77 AS patients and 61 controls were evaluated. Disease activity was evaluated by the BASDAI and ASDAS. Fatigue was evaluated with Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F), Fatigue Severity Scale (FSS) and fatigue-related item of the BASDAI. Fatigue was compared in AS and controls.

Results: A total of 63.6% of patients had severe fatigue measured by fatigue-related item of BASDAI and 42% of patients had severe fatigue measured by FFS. The 26.2% of controls had severe fatigue. FSS scores were 3.9 ± 2 in AS patients and 2.3 ± 1.3 in controls ($p < 0.05$). There was strong correlation between FSS and fatigue item of BASDAI ($r = 0.763$, $p < 0.05$) similarly there was strong correlation FACIT-F score and fatigue-related item of BASDAI ($r = -0.736$, $p < 0.05$). FFS score was 2.38 ± 1.46 in inactive AS patients and 4.87 ± 1.68 in active patients ($p < 0.05$). Fatigue was statistically significant correlated with pain, disease activity, depression, functional capacity and anxiety in AS ($p < 0.05$). BASDAI was an independent predictor of severe fatigue in AS ($p < 0.05$).

Conclusion: Severe fatigue is more common in AS, especially those with the active disease. Disease activity, functional abilities, depression and anxiety were correlated with fatigue. One of the FSS, FACIT-F and fatigue-related item of BASDAI scores are sufficient to evaluate fatigue

Keywords: fatigue, ankylosing spondylitis,

Özet

Amaç: Yorgunluk, Ankilozan spondilit (AS) hastalarında önemli bir semptomdur. AS'de yorgunluğu değerlendirmek için kabul edilmiş kesin bir ölçek yoktur. Çalışmanın amacı, AS'de yorgunluğu farklı ölçeklerle ölçmek ve yorgunluk ile ilgili değişkenleri bulmaktır.

Yöntem: 77 AS hastası ve 61 kontrol değerlendirildi. Hastalık aktivitesi BASDAI ve ASDAS ile değerlendirildi. Yorgunluk Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F), Fatigue Severity Scale (FSS) ve BASDAI'nin yorgunlukla ilişkili maddesi ile değerlendirildi. Yorgunluk AS ve kontrollerde karşılaştırıldı. Yorgunluk ile hastalıkla ilişkili parametrelerin korelasyonu değerlendirildi.

Bulgular: Hastaların %63.6'sında BASDAI'nin yorgunlukla ilgili maddesi ile ölçülen ve %42'sinde FFS ile ölçülen şiddetli yorgunluk vardı. Sağlıklı kontrollerin %26.2'sinde şiddetli yorgunluk vardı. FSS skoru AS hastalarında 3.9 ± 2 , kontrollerde 2.3 ± 1.3 idi ($p < 0.05$). FSS ile BASDAI'nin yorgunluk maddesi arasında güçlü bir korelasyon vardı ($r = 0.763$, $p < 0.05$), benzer şekilde FACIT-F ile BASDAI'nin yorgunluk maddesi arasında da güçlü bir korelasyon vardı ($r = -0.736$, $p < 0.05$). İnaktif AS hastalarında FFS skoru 2.38 ± 1.46 , aktif hastalarda 4.87 ± 1.68 idi ($p < 0.05$). Yorgunluk, AS'de ağrı, hastalık aktivitesi, depresyon, fonksiyonel kapasite ve anksiyete ile istatistiksel olarak anlamlı korelasyon vardı ($p < 0.05$). BASDAI, AS hastalarında şiddetli yorgunluğun bağımsız ön gördürücüsüyü ($p < 0.05$).

Sonuç: AS'de, özellikle aktif hastalığı olanlarda şiddetli yorgunluk daha yaygındır. Hastalık aktivitesi, fonksiyonel durum, depresyon, ağrı ve anksiyete yorgunluk ile ilişkilidir. BASDAI skorunun yorgunlukla ilgili maddesi, FSS, FACIT-F'den biri yorgunluğu değerlendirmek için yeterlidir.

Anahtar kelimeler: yorgunluk, ankilozan spondilit

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Introduction

Ankylosing Spondylitis (AS) is a chronic inflammatory rheumatic disease (1). Fatigue has been reported as one of the most common symptoms of AS, in addition to pain and stiffness (2). Fatigue is described as a lack of energy and exhaustion following an activity (3,4). Fatigue has been reported in various rheumatic diseases (5,6), and some previous studies have reported a frequency of fatigue at 53-63% in patients with AS (7,8). Fatigue is an important symptom for AS patients because it affects physical function, daily and social activities and causes morbidity (9), it has been reported as one of the main factors causing work instability in AS (10). Although one of the most important complaints reported by AS patients is fatigue, sufficient attention is not granted in the routine follow-ups and there is no definitively accepted scale to evaluate fatigue in patients with AS to date. In number of studies, fatigue in patients with AS has been evaluated solely using the question regarding fatigue in Bath ankylosing spondylitis disease activity index (BASDAI) (8,9,11). The purpose of the study was to assess levels of fatigue in AS and healthy controls by way of three different fatigue scales and to uncover variables related to severe fatigue in AS.

Material and Methods

In this cross-sectional study, 77 patients diagnosed with AS according to the Modified New York criteria (12) and 61 age and gender matched healthy hospital workers, were included. The G.POWER.3.1 program was used for power calculation. Subjects who had another an inflammatory rheumatic disease, fibromyalgia (FM), Diabetes mellitus, hyperlipidemia, hypertension, hypothyroidism, osteomalacia and psychiatric disorders, were excluded. The Visual Analogue Scale (VAS) was used to assess pain (13).

Disease activity was evaluated by using the BASDAI and the Ankylosing spondylitis disease activity score (ASDAS). ASDAS evaluated back pain, morning stiffness, joint involvement, patient general assessment in combination with laboratory parameters. ASDAS <1.3 indicates an inactive disease, ASDAS <2.1 indicates low disease activity, 2.1<ASDAS ≤ 3.1 indicates high disease activity and >3.1 indicates very high activity (14,15). BASDAI ≥ 4 is defined as an active disease (11).

Functionality was appraised with the Bath Ankylosing Spondylitis Functional Index (BASFI) (16). Quality of life was assessed with the Ankylosing Spondylitis Quality of Life (ASQoL) Scale (17). Depression and anxiety were evaluated by the Beck depression and Beck anxiety inventory respectively, higher scores showing more severe depression and anxiety (18,19).

Fatigue

Fatigue was evaluated using the Functional Assessment of

Chronic Illness Therapy (FACIT) -Fatigue Scale (FACIT-F) and Fatigue Severity Scale (FSS) and fatigue-related item of the BASDAI (first question of the BASDAI). The FSS consists of 9 items that evaluate social, cognitive and physical effects of fatigue. The scoring is accomplished by calculating the average of items. A value of 3 or higher indicates severe fatigue (20). Individuals with an FSS ≥ 3 or fatigue-related item of BASDAI ≥ 5 were classified as having severe fatigue. FACIT-F scale consists of 13-items which evaluate the effects of tiredness, weakness and lack of energy, daily functioning and sleep. Higher scores indicate higher functional status and less fatigue (21).

Permission for the study was obtained from the XXXX University Faculty of Medicine Ethics Committee, decision number 05-04 on 10/03/2021. Written informed consent was obtained from all participants.

The IBM SPSS version 22.0 was used for analysis and t-test was used to compare variables. Correlations between fatigue and clinical parameters were evaluated using Spearman correlation test. Binary logistic regression analysis was applied using the absence or presence of severe fatigue (according to the cutoff value of 3 for FSS and cut off value of 5 for the fatigue-related item of BASDAI) as the dependent variable to state predictors of severe fatigue.

Results

A total of 77 AS patients and 61 healthy controls were evaluated. The features of subjects are given in Table 1. The mean BASDAI and ASDAS were 4.5±2.12 and 2.91±1.05 respectively. Some 61% of patients with AS had an active disease according to the BASDAI (BASDAI ≥4). Otherwise, 2%, 22.1%, 36.4% and 39% of patients had inactive, low activity, high activity and very high disease activity respectively, according to ASDAS. There was 18.2% of patients who were receiving a sulfasalazine treatment, 18.2% were on biologics and 61% of were on nonsteroidal anti inflammatory drugs (NSAIDs).

The 63.6% of AS patients had severe fatigue as measured by fatigue related item of BASDAI and 42 % of AS patients had severe fatigue as measured by FFS. According to FFS 26.2% of controls had severe fatigue. According to fatigue item of BASDAI 36.1% of controls had severe fatigue. Severe fatigue was more common in AS patients (p<0.05).

FSS was 3.9±2 in AS patients and 2.3±1.3 in controls (p<0.05). The FFS score was 2.38±1.46 in inactive AS patients (BASDAI <4) and 4.87±1.68 in active AS patients (BASDAI ≥ 4). The FACIT-F score was lower in AS than in healthy controls (p<0.05). The FACIT-F score was 36.03±7.72 in inactive AS patients and 23.91±9.98 in active AS patients. Fatigue was higher in active disease compared to inactive disease (p<0.05).

Fatigue in AS patients was statistically significant correlated

with, pain, disease activity, functional capacity, depression and anxiety ($p<0.05$) (Table 2). Differences between fatigue groups are shown in Table 3. The FSS was strongly correlated with fatigue related item of BASDAI ($r=0.763$, $p<0.05$) and similarly, there was a strong correlation with the FACIT-F score and fatigue-related item from the BASDAI ($r=-0.736$, $p<0.05$).

Table 1. Characteristics of the patients and controls

	AS patients (n=77)	Healthy controls (n=61)	P value
Age	38.31±10.61	38.21±7.34	$p>0.05$
Gender(naun,percent)			
•Female	26 (33.8%)	19 (31.8%)	$p>0.05$
•Male	51 (66.2%)	42 (68.9%)	$p>0.05$
Marital status			
•Married	59 (76.6%)	49 (80.3%)	$p>0.05$
•Non married	18 (23.4%)	12 (19.7%)	$p>0.05$
Employment			
•Employed	51 (66.2%)	58 (95.1%)	$p<0.05$
•Unemployed	26 (33.8%)	3 (4.9%)	$p<0.05$
Smoking			
•Smoking	28 (36.6%)	12 (19.6%)	
•No smoking	49 (63.4%)	49 (80.32%)	
Disease duration (year)	9.7±8.13	-	
Fatigue item of BASDAI (range: 0–10)	5.23±2.49	3.82±1.99	$p<0.05$
FACIT-F	28.63±10.88	36.31±8.73	$p<0.05$
FSS	3.9±2	2.3±1.3	$p<0.05$
Beck Depression score	12.38±8.68	6.06±8.07	$p<0.05$
Beck Anxiety score	14.68±10.66	6.32±6.75	$p<0.05$
BASDAI (range: 0–10)	4.5±2.12	-	
ASDAS	2.91±1.05	-	
BASFI (range: 0–10)	3.55±2.86	-	
C-reaktif protein (mg/dL)	0.95±1.76	-	

Binary logistic regression demonstrated that BASDAI is an independent predictor of severe fatigue in AS patients (according to BASDAI fatigue item ≥ 5 , OR: 2.836, $p<0.05$) (according to FSS ≥ 3 : OR:3.453 $p<0.05$) (Table 4,5).

Discussion

This study was performed to evaluate the fatigue in AS patients and healthy controls using three different scales and to evaluated the relation between disease-related parameters and fatigue in AS. Fatigue was found to be more common in AS patients. In previous studies, fatigue has been generally assessed with the fatigue related-item of the BASDAI (8,9). Therefore this study differentiates itself from others that have evaluated fatigue in patients with AS, because fatigue was assessed with three different scores. Indeed fatigue was evaluated by FSS and FACIT-F as well as the fatigue-related item of BASDAI. The 63.3% of AS patients had severe fatigue defined as per the BASDAI fatigue score ≥ 5 and 54.5% of AS

patients were found the have severe fatigue defined as FSS ≥ 3 . Patients with AS had lower FACIT-F scores compared to healthy controls and also, active AS patients had lower scores than inactive AS patients. This results supported that healthy controls and non active AS patients had less fatigue. There was a the strong correlation between FSS, FACIT-F and fatigue-related item of BASDAI. This result suggests that using one of these scores in future studies may be sufficient to evaluate fatigue in patients with AS.

Table 2. Correlation analysis results of AS patients.

	FSS	FACIT-F	fatigue item of BASDAI
BASDAI	$r= 0.750$ $p<0.05$	$r= -0.735$ $p<0.05$	$r= 0.785$ $p<0.05$
ASDAS	$r=0.400$ $p<0.05$	$r= 0.388$ $p<0.05$	$r= 0.478$ $p<0.05$
BASFI	$r= 0.590$ $p<0.05$	$r= 0.581$ $p<0.05$	$r= 0.533$ $p<0.05$
ASQUEL	$r= 0.642$ $p<0.05$	$r= - 0.600$ $p<0.05$	$r= 0.569$ $p<0.05$
BECK Depression	$r= 0.475$ $p<0.05$	$r= -0.548$ $p<0.05$	$r= 0.349$ $p<0.05$
BECK Anxiety	$r= 0.528$ $p<0.05$	$r= - 0.704$ $p<0.05$	$r= 0.472$ $p<0.05$
VAS ağrı	$r= 0.353$ $p<0.05$	$r= 0.420$ $p<0.05$	$r= 0.385$ $p<0.05$
CRP	$r= 0.004$ $p>0.05$	$r=0.180$ $p>0.05$	$r= 0.08$ $p>0.05$

Fatigue has been reported to be related with disease activity in studies evaluating BASDAI as the disease activity score (8). In most studies related with AS, disease activity was evaluated with only BASDAI. In this study, disease activity was assessed with using both BASDAI and ASDAS and it was observed that fatigue was strongly correlated with both activity scores. AS patients were grouped as active and inactive disease according to BASDAI. The majority of patients had active disease and it was also found that active AS patients had more severe fatigue. It was found that BASDAI predicted severe fatigue in AS patients evaluated by the FSS scale and the BASDAI fatigue-related item. Consistently with these results Zhou et al. reported that BASDAI was an independent predictive factor for fatigue assessment by FSS (4).

Table 3: Differences between fatigue group with respect to the disease specific measures.

	BASDAI fatigue item ≥ 5	BASDAI fatigue item < 5	p	FSS ≥ 3	FSS<3	P value
Fatigue item of BASDAI	6.77±1.59	2.53±1.07	$p<0.05$	6.76±1.89	3.4±1.89	$p<0.05$
BASDAI	5.55±1.77	2.89±1.54	$p<0.05$	5.86±1.66	3.04±1.5	$p<0.05$
ASDAS	3.16±0.99	2.47±1.01	$p<0.05$	3.32±0.8	2.4±1.08	$p<0.05$
BASFI	4.46±2.96	1.9±1.72	$p<0.05$	5.01±2.82	1.75±1.63	$p<0.05$
ASQoL	10.02±4.44	5.28±4.55	$p<0.05$	11.04±3.9	5±4.07	$p<0.05$
Beck depression	14.35±7.88	9±9.07	$p<0.05$	15.87±8.9	8.2±6.3	$p<0.05$
Beck anxiety	17.55±11.25	9.67±7.34	$p<0.05$	19.09±11.3	9.4±6.8	$p<0.05$
FACIT	23.42±9.33	37.7±6.56	$p<0.05$	21.76±9.08	36.8±6.05	$p<0.05$
FSS	4.92±1.7	2.13±0.97	$p<0.05$	5.48±1.22	2.01±0.6	$p<0.05$

FM has been commonly reported in patients with AS. The co-

existence of AS and FM leads to confusion in patient-reported results of disease on account of overlapping symptoms (22). Therefore in this study, to avoid confusion, patients had fibromyalgia were not included.

Table 4: Factors related with the presence of severe fatigue (FSS ≥ 5) in AS patients by binary logistic regression analysis.

	β	S.E	Wald	Sig	Exp (B)	95 % CI
Age	0.046	0.054	0.729	0.393	1.047	0.942-1.165
Disease duration	-0.010	0.072	0.018	0.893	0.990	0.860-1.140
VAS pain	-0.188	0.201	0.873	0.350	0.829	0.559-1.229
BASDAI	1.239	0.533	5.404	0.02	3.453	1.215-9.817
ASDAS	-0.668	0.825	0.655	0.418	0.513	0.102-2.583
BASFI	0.288	0.309	0.866	0.352	1.334	0.727-2.445
Beck Anxiety	-0.015	0.067	0.053	0.818	0.985	0.864-1.122
Beck depression	0.146	0.068	4.632	0.03	1.157	1.013-1.321
ASQoL	0.059	0.136	0.188	0.665	1.061	0.813-1.383
CRP	0.402	0.379	1.124	0.289	1.495	0.711-3.144

Table 5: Factors related with the presence of severe fatigue (BASDAI related item ≥ 5) in AS patients by binary logistic regression analysis

	β	S.E	Wald	Sig	Exp (B)	95 % CI
Age	-0.025	0.029	0.701	0.403	1.025	0.968-1.085
Disease duration	-0.018	0.037	0.247	0.619	0.982	0.913-1.056
VAS pain	0.175	0.095	3.396	0.06	1.191	0.989-1.434
BASDAI	1.042	0.456	5.230	0.022	2.836	1.161-6.928
ASDAS	-0.506	0.482	1.102	0.294	0.603	0.235-1.550
BASFI	0.071	0.271	0.069	0.793	1.074	0.631-1.828
Beck Anxiety	-0.068	0.078	0.741	0.389	0.935	0.801-1.090
Beck depression	-0.025	0.060	0.173	0.678	0.975	0.867-1.097
ASQoL	-0.173	0.169	1.042	0.307	0.841	0.604-1.172
CRP	-0.005	0.135	0.001	0.970	0.995	0.763-1.297

In the present study, functional disability was found to be related with fatigue and AS patients with severe fatigue had worse functionality. Turan et al. found similar result (23). The relationship between fatigue and acute phase reactants is still unclear. Dagwnrud et al. reported that there was no

relationship between fatigue and CRP (24). In concordance with this result there was no relation between fatigue and ESR and CRP in this study.

Dernis-Labous et al. showed that nonsteroidal anti-inflammatory drug therapy did not have a significant effect on reducing fatigue (9). Bedaiwi et al. found significant but weak relation between CRP and fatigue. In their study fatigue persisted in majority of patients, although there was a significant decrease in FSS by using TNFi therapy (25). Although most of the AS patients used NSAIDs, the frequency of severe fatigue was quite high in this study. On the other hand, CRP was not found to be an independent predictor of severe fatigue. This result supports that the role of inflammation is still unclear in severe fatigue and there is a need for studies explaining the relation between inflammation and fatigue.

Quality of life is significantly reduced in AS (26). In our study patients with severe fatigue had a lower quality of life and the frequency of depression was higher in AS. There was a significant relationship between fatigue and depression. Aissaoui et al. reported that compared with non-fatigue patients, fatigue patients had more significant anxiety and depression (27).

In conclusion, this study had shown that severe fatigue was more common in AS patients, in particular those with active disease. Disease activity, functional abilities, depression, pain and anxiety were significantly correlated with fatigue in patients with AS. BASDAI was the main independent factor that predicted fatigue. The effect of inflammation is still unclear in severe fatigue and studies evaluating the relationship between inflammation and fatigue in patient with AS are needed. One of FSS, FACIT-F and fatigue-related item of BASDAI scores is sufficient to evaluate fatigue.

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