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Original Article

The Factors Related to Work Productivity and Disease Costs in Patients with Ankylosing Spondylitis

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Abstract

Background: To examine the effect of ankylosing spondylitis (AS) on work productivity, work instability and absenteeism, and the cost to the national economy of the disease.

Methods: This cross-sectional study included 100 AS patients from the outpatient rheumatology clinic at Akdeniz University Hospital who met the 1984 modified New York criteria. Annual direct and indirect care costs of the AS patients were recorded, along with their sociodemographic data and clinical characteristics. Direct costs were based on reimbursements from the National Social Security Institution, while indirect costs were estimated using the human capital approach to account for productivity loss and absenteeism related to income, reflecting the disease's economic impact on work capabilities. The work-related outcomes were evaluated with the Work Productivity and Activity Impairment-Spondyloarthropathy (WPAI-SpA) and Ankylosing Spondylitis Work Instability Scale (AS-WIS). Pearson correlation analysis was applied to determine the relationships between quantitative variables, while the Chi-square test or Fisher's exact test was used for relationships between qualitative variables. To assess the effects of independent variables on work productivity impairment, activity, and work instability, multivariate linear and logistic regression methods were used.

Results: Among the 87 working AS patients, 38 (43.7%) exhibited moderate to high work instability (AS-WIS ≥ 11). These patients had higher rates of absenteeism, presenteeism, overall work impairment, daily activity impairment, and scores for Ankylosing Spondylitis Disease Activity Score-C Reactive Protein (ASDAS-CRP), Bath Ankylosing Spodylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), The Ankylosing Spondylitis Quality of Life, and PG-VAS. Ankylosing spondylitis patients had an average absence of 10.3 working days in the past year. Their annual healthcare costs averaged €3782.76, primarily due to medication costs of €3674.89. Among the 87 working AS patients, 10 (11%) reported productivity losses in the last year, totaling €1059.62. The AS-WIS score showed moderate to high correlations with presenteeism, daily activity impairment, overall work impairment, BASDAI, PG-VAS, BASFI, and ASDAS-CRP. In contrast, absenteeism had weak correlations with BASMI and CRP, moderate correlation with overall work impairment, and no correlation with BASDAI and BASFI. Lateral spine mobility, quality of life, educational level, BASFI and BASMI scores, smoking, and the work performed were predictors of work instability and impairment in work productivity.

Conclusions: In addition to healthcare costs, the costs related to unemployment, absenteeism, and loss of productivity constitute a significant proportion of the total costs, and it was seen that AS has a negative effect on the economy of the country. If work instability and impairment in work productivity are identified early, the risk of work disability can be reduced or eliminated with appropriate clinical and workplace interventions.

Keywords: Ankylosing spondylitis, absenteeism, sick leave, cost of illness

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Introduction

Axial, articular, and extra-articular involvements related to ankylosing spondylitis (AS) cause severe economic losses together with diminished quality of life for the patient and reduced work productivity.[1]

In the international guidelines of the Canada Rheumatology Association and the Canada Spondyloarthritis Research Institute, it is recommended to include work activities in disease follow-up.[2] Loss of work productivity, work instability, and work disability are work-related outcome measures widely used in AS patients.[3] Work disability is usually defined as work inability due to health problems. While work disability is a term defining absenteeism, it does not define the limitations and difficulties causing loss of work productivity in AS patients. This period before work disability is referred to as work instability, which can be defined

as incompatibility between the functional and cognitive abilities of the employee and the requirements of the job.[4] As AS starts at an early age and causes significant problems related to loss of work productivity and work disability, the lifetime economic burden is large.[5]

In some previous studies, the factors affecting work-related outcomes have been examined.[1,6-10] To date, no consensus has been reached on the subject of which dependent factors, as independent health-related variables, have a significant effect on these outcomes. The economic burden of AS in Turkey has not been documented. The aim of the current study was to determine the effect of many health and work-related variables of AS patients on work productivity, work instability, and absenteeism, and to examine the costs to the economy of the country of the disease.

Material and Methods

This cross-sectional, single-center study included patients consecutively selected from the rheumatology unit of Akdeniz University Hospital in Turkey between November 2021 and March 2022. The study included 100 patients who were diagnosed with AS according to the modified New York criteria.[11] The study exclusion criteria were defined as age <18 years or >65 years, or the presence of an additional rheumatismal disease, severe infection, or malignancy, which were expected to increase associated costs and limitations in working life.

Approval for the study was granted by the Clinical Research Ethics Committee of Akdeniz University School of Medicine (decision no.: 70904504/626, dated: October 04, 2021). Written informed consent was obtained from all patients in accordance with the ethical principles for medical research involving human subjects as outlined in the Helsinki Declaration.

Main Points

- In addition to healthcare-related costs, work-related costs (unemployment, absenteeism, loss of work productivity) form a large part of the AS-related economic burden.
- It seems to be necessary to evaluate the risk of work instability in AS patients because of its high prevalence of work instability.
- Lateral spine mobility, quality of life, educational level, the BASFI score, the BASMI score, smoking, and the work performed were found to be predictors of work instability and work productivity.

The sociodemographic data and clinical characteristics of the patients were recorded. The patients were questioned about their work status and the types of work were classified as physical or clerical. Physical work included manual workers, tradesmen, shop owners, and farmers. Clerical work included salaried employees in finance and administration, engineers, drivers, artists, teachers, lawyers, and healthcare workers.

In the evaluation of AS disease activity, the Bath Ankylosing Spodylitis Disease Activity Index (BASDAI)[12] and Ankylosing Spondylitis Disease Activity Score-C Reactive Protein (ASDAS-CRP)[13] were used. Functional capacity of the patients was evaluated using the Bath Ankylosing Spondylitis Functional Index (BASFI),[14] spinal and hip mobility with the Bath Ankylosing Spondylitis Metrology Index (BASMI),[15] and quality of life with The Ankylosing Spondylitis Quality of Life (ASQoL)[16] scale.

In the evaluation of work-related outcome measures, the Work Productivity and Activity Impairment-Spondyloarthropathy (WPAI-SpA)[17,18] and the Ankylosing Spondylitis Work Instability Scale (AS-WIS)[19,20] were applied. The WPAI-SpA is a questionnaire consisting of 6 items evaluating the effects of AS on work and daily activities in the last 7 days. This questionnaire evaluates 4 parameters of absenteeism (WPAI-1), presenteeism (WPAI-2, impairment while working), overall work impairment (WPAI-3), and daily activity impairment (WPAI-4). Higher scores indicate a greater loss of productivity and activity. From the responses given to the questions in the WPAI-SpA questionnaire, special formulas were used to calculate absenteeism [Q2/(Q2 + Q4)], presenteeism (Q5/10), overall work impairment [Q2/(Q2 + Q4) + ((1−Q2/(Q2 + Q4)) × (Q5/10))] and daily activity impairment (Q6/10). The final score is obtained as a percentage by multiplying the results by 100.

Ankylosing Spondylitis Work Instability Scale is used to determine work instability. This is a questionnaire of 20 disease-specific questions, which determines the work instability as low (<11), moderate (11-18), or high risk (19-20).[19] The AS-WIS was translated, cross-culturally adapted, and validated in Turkish.[20] In this study, the patients were grouped as low work instability risk <11 points and moderate-high work instability risk ≥11 points according to the AS-WIS scores.

In the evaluation of AS costs, direct and indirect costs were calculated. In the calculation of the direct costs, reimbursements from the national social security institution were taken into consideration. The costs of medications prescribed for AS treatment were comprehensively collected. This included paracetamol, topical and oral non-steroidal anti-inflammatory drugs, glucocorticoids, conventional disease-modifying anti-rheumatic drugs, and anti-tumor necrosis factor-alpha (anti-TNF) drugs. Notably, none of the patients received JAK inhibitors or anti-IL-17 treatments during the study period. The costs for tests encompassed both laboratory tests and imaging tests, such as X-ray and magnetic resonance imaging. For calculating the costs of loss of productivity and absenteeism, income levels were taken into consideration, and the human capital approach was used. Cost minimization has not been applied, and adjustments for purchasing power parity have not been made. All costs are based on data from 2021 and 2022.

Sample Size and Statistical Analysis

To ensure the adequacy of our sample size, we performed a sample size calculation using the following formula:

$$n = \frac{\left(Z_{\left\{\frac{\alpha}{2}\right\}} \times \sigma\right)^2}{E}$$

- Confidence Level**:** 95% (thus, $Z_{\left\{\frac{\alpha}{2}\right\}} = 1.96$)
- Margin of Error €**:** 5% (0.05)
- The standard deviation (σ) was calculated as 0.4984 using the prevalence of AS in the Turkish population.

Data obtained in the study were analyzed statistically using SAS 9.4 software. Descriptive statistics were stated as mean ± standard deviation (SD) for quantitative variables and as number (n) and percentage (%) for categorical variables. Conformity of the data to normal distribution was assessed with the Shapiro–Wilk test and skewness coefficients were examined. As the data did not show normal distribution, non-parametric tests were used in the statistical analyses. In the paired comparisons of two categorical variables, the Kruskal–Wallis test was used for independent groups, and to be able to determine differences between three or more groups, Mann–Whitney analysis was applied. Pearson correlation analysis was performed to determine relationships between quantitative variables, and the Chi-square or Fisher's exact test was used for relationships between categorical variables. To examine whether or not independent variables had an effect on quantitative and dichotomous dependent variables, multivariate stepwise

simple linear and logistic regression methods were used consecutively, and by discarding ineffective variables, the variables significant for dependent variables were determined. To ensure the validity of the multivariate linear regression models, multicollinearity was assessed using variance inflation factors (VIFs) and tolerance values, with acceptable thresholds set at VIF <10 and tolerance >0.1. Additionally, the White test was used to verify the assumption of constant variance in the regression models. A value of $P < .05$ was accepted as statistically significant in all the study analyses.

Results

Evaluation was made of 100 patients with AS, comprising 85 (85%) males and 15 (15%) females with a mean age of 40.3 ± 10.1 years. Of the total patients, 87 (87%) were actively working, and 13 (13%) were not working.

AS-related work disability was reported by 1 (6.6%) female and 6 (7.0%) males. The duration of work disability specifically due to AS was reported as 3.0 ± 0.9 years by the female and as 5.8 ± 5.0 years by the males ($P = .799$).

Gender differences were present in the BASDAI score, which was higher in females ($P = .020$), and in the BASMI score, which was higher in males ($P = .012$). No difference was determined between the genders with respect of the CRP level and ASDAS-CRP, the BASFI score, and the ASQoL score. A lower percentage of female patients (66.7%) than male patients (88.2%) were determined to have been prescribed anti-TNF ($P = .031$).

The mean AS-WIS score was determined to be 9.5 ± 5.6. Based on these scores, patients were categorized into groups and compared with respect to sociodemographic, clinical characteristics, absenteeism, and work productivity (Tables 1 and 2). Absenteeism of the AS patients was determined as a mean 10.3 working days in the last year (10.3 working days lost/patient/year).

No significant difference was determined between the AS-WIS groups in respect of mean CRP levels and BASMI scores ($P > .05$). The BASDAI, ASDAS-CRP, BASFI, and ASQoL scores were determined to be higher in the group with a moderate-high risk of work instability ($P < .001$). According to the BASDAI score in the group with a moderate-high risk of work instability, disease activity was 55.3%, and this rate was determined as 20.4% in the low-risk group ($P < .001$).

Table 1. The Relationships of the Sociodemographic and Clinical Characteristics of the AS Patients with the AS-WIS Scores

	All Patients n = 100	AS-WIS <11 n = 49	AS-WIS ≥11 n = 38	*P*
Age (years), mean (SD)	40.3 (10.1)	36.9 (8.2)	39.8 (8.9)	.114
Gender: male, n (%)	85 (85.0%)	41 (83.7%)	32 (84.2%)	.946
Disease duration, (years) mean (SD)	12.8 (9.5)	11.5 (8.0)	10.9 (7.7)	.680
Education level, n (%)				.223
Middle school and below	26 (26.5%)	9 (18.8%)	13 (35.1%)	
High school	32 (32.7%)	16 (33.3%)	9 (24.3%)	
University and above	40 (40.8%)	23 (47.9%)	15 (40.5%)	
Smoking status: active smoker, n (%)	45 (45.0%)	21 (42.9%)	19 (50.0%)	.507
Family history of AS, n (%)	35 (35.0%)	15 (30.6%)	15 (39.5%)	.388
Uveitis history, n (%)	28 (28.0%)	13 (26.5%)	7 (18.4%)	.372
IBD history, n (%)	6 (6.0%)	4 (8.2%)	2 (5.3%)	.596
Anti-TNF-α use, n (%)	85 (85.0%)	41 (83.7%)	33 (86.8%)	.680
AS-related surgery, n (%)	4 (4.0%)	3 (6.1%)	1 (2.6%)	.440
PG-VAS, mean (SD)	3.9 (2.3)	2.9 (1.9)	5.1 (2.2)	<.001
Change of job because of AS, n (%)				.634
Yes	14 (14.0%)	6 (12.2%)	6 (15.8%)	
No	86 (86.0%)	43 (87.8%)	32 (84.2%)	
Daily activity impairment, %, mean (SD)	31.8 (26.5)	18.0 (17.4)	47.4 (24.7)	<.001

Anti-TNFα, anti-tumor necrosis factor-alpha; AS, ankylosing spondylitis; AS-WIS, Ankylosing Spondylitis Work Instability Scale; IBD, Inflammatory Bowel Disease; PG-VAS, Patient Global Visual Analogue Scale; SD, standard deviation.

The costs related to AS per patient per year are shown in Table 3. The annual healthcare costs of the AS patients were determined as 3782.7 Euros (€) (Euro exchange rate of 10.4 as the average for 2021). The most substantial part of the total costs was the cost of medications (97.1%). This was followed by the costs of tests (1.2%), outpatient visits (0.8%), physiotherapy for 5% of the patients (0.5%), consultations (0.3%), day-patients (0.1%), and hospitalized patients (0%).

Of the 87 working patients, 10 (11%) described loss of productivity in the last year, which incurred a cost of €1059.6. AS-related absenteeism was reported by 72 (83%) patients at a cost of €313.4. A mean cost of €368.4 related to special expenses and carers was reported by 34 (34%) patients. Loss of earnings due to AS-related retirement was stated by 2 (2%) patients, and work disability because of AS-related health problems by 1 (1%) patient, incurring mean costs of €122.6. The cost of transport-accommodation was found to be a mean €27.2.

When the patients were grouped according to the BASDAI scores, anti-TNF-α was determined to be used by 74.3% of the patients with a BASDAI score ≥4 and by 90.8% of the patients with a BASDAI score <4 ($P = .027$).

Table 4 shows the correlation of the data evaluated in the study with each other.

All multivariate linear regression models satisfied the assumption of no multicollinearity, as indicated by VIF values below 10 and tolerance values above 0.1 (see Table 5). The average errors for these models were 0.00 ± 1.00. The White test results for the 5 regression models were as follows: $\chi^2(9) = 15.00$, $P = .091$; $\chi^2(14) = 10.56$, $P = .720$; $\chi^2(9) = 7.96$, $P = .538$; $\chi^2(26) = 20.07$, $P = .788$; $\chi^2(19) = 14.12$, $P = .776$. All *P*-values indicate that the null hypothesis of constant variance is accepted, confirming that the models meet the assumption of constant variance.

Discussion

The results of this study demonstrated that of the 87 working AS patients included in the

Table 2. Relationships Between the Risk of Work Instability and Work Characteristics, Absenteeism, and Work Productivity

		AS-WIS		
	Working Patients n = 87	<11 n = 49	≥11 n = 38	*P*
Duration of working (years), mean (SD)	16.3 (7.5)	14.9 (7.2)	18.2 (7.4)	.029
Work performed, n (%)				.653
Physical	48 (55.2%)	26 (53.1%)	22 (57.9%)	
Clerical	39 (44.8%)	23 (46.9%)	16 (42.1%)	
Absenteeism from work in the last year (days), mean (SD)	10.3 (20.5)	5.1 (7.7)	16.9 (28.6)	.004
Absenteeism from work in the last year, n (%)				.122
1-30 days	80 (92.0%)	47 (95.9%)	33 (86.8%)	
31-120 days	7 (8.0%)	2 (4.1%)	5 (13.2%)	
Absenteeism from work in the last week (hrs), mean (SD)	2.8 (9.5)	2.4 (10.5)	3.4 (8.3)	<.001
Absenteeism, %, mean (SD)	7.4 (22.3)	5.1 (21.0)	10.4 (24.0)	<.001
Presenteeism, %, mean (SD)	33.8 (27.2)	18.8 (19.8)	53.2 (23.1)	<.001
Overall work impairment, %, mean (SD)	38.6 (31.0)	23.0 (25.8)	58.1 (25.6)	<.001

AS-WIS, Ankylosing Spondylitis Work Instability Scale; SD, standard deviation.

Table 3. The AS-Related Costs Per Patient and the Distribution of Costs According to the BASDAI Scores

		BASDAI Score		
	All Patients Mean (SD) n = 100	Mean (SD) BASDAI < 4 n = 65	BASDAI ≥ 4 n = 35	*P*
Outpatient visits	30.1 (24.1)	27.3 (19.1)	35.4 (30.9)	.183
Medications	3674.8 (2268.1)	4030.5 (201.4)	3014.4 (2476.5)	.039
Tests	44.0 (35.4)	43.2 (35.7)	45.5 (35.3)	.580
Physiotherapy	17.7 (94.2)	23.5 (113.3)	7.0 (38.7)	.855
AS-related consultations	10.1 (13.0)	11.6 (14.5)	7.4 (9.4)	.347
Day patient admission	5.6 (8.8)	6.6 (9.1)	3.8 (7.9)	.213
Total direct costs	3782.7 (2284.4)	4142.9 (2090.8)	3113.7 (2501.4)	.039
Early retirement—work disability	122.6 (729.4)	50.2 (405.1)	257.0 (1100.7)	.240
Absenteeism, n = 87	313.4 (1456.6)	66.6 (219.3)	761.3 (2382.0)	.162
Special expenses, carer	368.4 (2880.1)	4873.1 (465.4)	188.4 (603.2)	.017
Transport-accommodation	27.2 (41.0)	25.0 (42.7)	31.2 (37.8)	.229
Loss of productivity, n = 87	1059.6 (6324.6)	1386.9 (7738.5)	459.6 (2074.3)	.695
Total indirect costs	1712.9 (9001.0)	1796.1 (10693.3)	1558.2 (4541.5)	.009

AS, ankylosing spondylitis; BASDAI,Bath Ankylosing Spondylitis Disease Activity Index; SD, standard deviation.

study, 38 (43.7%) had a moderate-high risk of work instability. The rates of absenteeism, presenteeism, overall work impairment, and daily activity impairment, the specific disease markers (ASDAS-CRP, BASDAI, BASFI), and the ASQoL and Patient Global Visual Analogue Scale (PG-VAS) scores were determined to be higher in the patients with a moderate-high risk of work instability. Therefore, if the disease activity and general health conditions in AS are improved, work instability may potentially be reduced.

In a study by Reilly et al[17] of AS patients, mean absenteeism was determined as 9.0%, presenteeism as 41.7%, overall work impairment as 43.9%, and daily activity impairment as 54.9%. In the current study, mean absenteeism was determined as 7.4%, presenteeism as 33.8%, overall work impairment as 38.6%, and daily activity impairment as 31.8%. Of the total working patients, 17 (19.5%) reported absenteeism in the last week, and 67 (77%) presenteeism, while 78 (78%) of all the patients reported daily activity impairment in the last week.

Taser et al[3] reported moderate-high work instability in 40% of AS patients, which was a similar rate to the 43.7% found in the current study. In that study, the AS-WIS score was found to be correlated at a moderate level with the BASDAI, BASFI, and PG-VAS scores. Similarly, in the current study, the AS-WIS score was found to be correlated at a moderate-high level with presenteeism, daily activity impairment, overall work impairment, BASDAI, PG-VAS, BASFI, and ASDAS-CRP scores.

Öncü et al[21] reported that the correlation between WPAI-1 and the BASDAI score and job satisfaction was highly significant. In this study, with the exception of heavy lifting, no correlation was determined between any of the work-related physical factors and WPAI-1. In the current study, a weak correlation was determined between WPAI-1 and the BASMI score and CRP, a moderate correlation between WPAI-1 and overall work impairment, and no correlation was found with the BASDAI and BASFI scores.

Macfarlane et al[22] reported that work disability was most strongly correlated with previous absenteeism, and absenteeism was most strongly related to previous presenteeism, physically intensive work, and peripheral joint involvement. In that study, it was found that

Table 4. Correlation of Data Evaluated in the Study

	ASWIS	WPAI-1	WPAI-2	WPAI-3	WPAI-4	BASMI	BASFI	BASDAI	ASDAS-CRP	CRP, mg/L	PG-VAS	Back Pain	Morning Stiffness	Peripheral Involvement
ASWIS	1.000													
WPAI-1	0.155 0.161	1.000												
WPAI-2	0.708 <0.001	0.155 0.161	1.000											
WPAI-3	0.632 <0.001	0.570 <0.001	0.878 <0.001	1.000										
WPAI-4	0.645 <0.001	0.104 0.342	0.605 <0.001	0.525 <0.001	1.000									
BASMI	0.230 0.031	0.217 0.046	0.393 <0.001	0.449 <0.001	0.302 0.002	1.000								
BASFI	0.536 <0.001	0.085 0.441	0.596 <0.001	0.532 <0.001	0.665 <0.001	0.619 <0.001	1.000							
BASDAI	0.582 <0.001	0.073 0.507	0.489 <0.001	0.394 <0.001	0.525 <0.001	0.080 0.424	0.597 <0.001	1.000						
ASDAS-CRP	0.508 <0.001	0.196 0.073	0.489 <0.001	0.476 <0.001	0.474 <0.001	0.218 0.029	0.582 <0.001	0.827 <0.001	1.000					
CRPmgL	0.085 0.429	0.308 0.004	0.128 0.237	0.261 0.016	0.075 0.459	0.123 0.221	0.158 0.116	0.150 0.135	0.493 <0.001	1.000				
PG-VAS	0.555 <0.001	0.100 0.360	0.557 <0.001	0.489 <0.001	0.547 <0.001	0.268 0.007	0.641 <0.001	0.793 <0.001	0.802 <0.001	0.155 0.122	1.000			
Back pain	0.468 <0.001	0.051 0.642	0.412 <0.001	0.320 0.003	0.481 <0.001	0.100 0.320	0.490 <0.001	0.825 <0.001	0.789 <0.001	0.021 0.829	0.697 <0.001	1.000		
Morning stiffness	0.339 0.001	0.008 0.939	0.367 <0.001	0.301 0.005	0.221 0.027	0.125 0.212	0.291 0.003	0.455 <0.001	0.468 <0.001	0.017 0.863	0.437 <0.001	0.447 <0.001	1.000	
Peripheral involvement	0.330 0.001	0.124 0.259	0.245 0.021	0.241 0.027	0.308 0.001	-0.002 0.97	0.359 <0.001	0.659 <0.001	0.551 <0.001	0.246 0.013	0.498 <0.001	0.323 0.001	0.071 0.476	1.000

ASDAS, Ankylosing Spondylitis Disease Activity Score; AS-WIS, Ankylosing Spondylitis Work Instability Scale; BASFI, Bath Ankylosing Spondylitis Functional Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CRP, C-reactive protein; PG-VAS, Patient Global Visual Analogue Scale; WPAI, Work Productivity and Activity Impairment.

Table 5. Predictive Factors for Impairment of Work Productivity and Activities and Work Instability

Variables	β	95% Lower CI	95% Upper CI	P	Tolerance	VIF
ASWIS						
Intercept	0	2.901	5.626	<.001	.	0
Lateral lumbar spine mobility	-0.206	-0.792	-0.119	.008	0.807	1.237
ASQoL	0.448	0.322	0.738	<.001	0.607	1.646
Presenteeism	0.522	0.069	0.140	<.001	0.610	1.638
Absenteeism						
Intercept	0	1.616	25.140	.026	.	0
Absenteeism in the last year	0.672	0.546	0.895	<.001	0.915	1.092
CRP, mg/L	0.237	0.222	1.141	.004	0.942	1.060
Presenteeism						
Intercept	0	1.773	30.280	.028	.	0
Education level	-0.205	-11.684	-2.119	.005	0.928	1.076
BASFI	0.273	1.360	5.310	.001	0.714	1.400
ASWIS	0.529	1.800	3.375	<.001	0.723	1.383
Overall work impairment						
Intercept	0	-65.056	-1.313	.041	.	0
Clerical work	-0.188	-20.116	-3.542	.005	0.946	1.056
Absenteeism in the last year	0.308	0.253	0.657	<.001	0.884	1.130
No change of job because of AS	0.170	3.673	27.293	.010	0.977	1.023
Smoker	0.147	1.120	17.303	.026	0.990	1.010
BASMI	0.285	2.945	8.133	<.001	0.925	1.080
ASWIS	0.476	1.916	3.475	<.001	0.873	1.145
Daily activity impairment						
Intercept	0	3.183	33.965	.018	.	0
ASQoL	0.230	-0.071	2.571	.063	0.339	2.942
BASFI	0.356	1.653	6.335	.001	0.463	2.156
ASWIS	0.330	0.604	2.367	.001	0.526	1.900

ASQoL, Ankylosing Spondylitis Quality of Life; AS-WIS, Ankylosing Spondylitis Work Instability Scale; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CRP, C-reactive protein; mg/L, milligrams per liter.

high disease activity, physically intensive work, and weaker physical function were independently correlated with future presenteeism. In the current study, work instability was found to be predicted by a decrease in lateral lumbar spine mobility, a high ASQoL score, and presenteeism. Absenteeism was found to be predicted by an increase in CRP level and presenteeism by a decrease in education level and an increase in BASFI and AS-WIS scores.

Ward and Kuzis[23] could not confirm that there was a correlation between absenteeism and physically difficult work. In a study by Boonen et al[24] the BASFI score was seen to be related to periods of absenteeism independently of physical work. Although no relationship was determined between physical work and absenteeism in the current study, the overall work impairment was seen to be lower in those who performed clerical work.

The study conducted by Zhao et al[25] aimed to investigate whether the association between socioeconomic factors and work outcomes in spondyloarthritis is modified at the country level according to individual-level socioeconomic factors. It included a total of 3835 patients from 23 countries worldwide (61% male). Employment status was found to be non-linearly associated with gender (male vs. female OR 2.5; 95% CI 1.9-3.2), education (university vs. primary school OR 3.7; 2.9-4.7), and marital status (married vs. single OR 1.3; 1.04-1.6). University education (compared to primary education) was associated with lower rates of absenteeism (OR 0.7; 0.5-0.96) and presenteeism (OR 0.5; 0.3-0.7). Higher health care expenditure (HCE) was associated with more favorable work outcomes (e.g. a higher probability of employment). Gender inequality in employment rates was found to be higher in countries with lower socioeconomic development. In a study conducted by Rodrigues Manica et al[26] across 22 countries worldwide, higher education or living in a country with higher HCE or human development index (HDI) was positively associated with being employed. However, no significant relationship was found between individual-level and country-level socioeconomic factors and absenteeism or presenteeism. In the current study, it was found that presenteeism decreases as the level of education increases. However, no differences were found in employment rates between genders, possibly due to the high participation of male patients (85%).

Akkoç et al[27] calculated the mean annual healthcare costs for AS patients to be €4335.2. The most significant part of the total costs was the cost of medication (€4032.7), while the loss of workdays cost mean of €414.1. In the current study, the mean annual healthcare costs for the AS patients were calculated as €3782.7, with the most important component being the cost of medications (€3674.8). The reason for the lower costs in this study compared to previous reports could be that, as it was conducted during the COVID-19 pandemic, fewer AS patients presented at the hospital during that period and some may have taken a break from their medications.

Malhan et al[28] calculated the total annual cost for an AS patient, combining both direct and indirect costs, to be €10 555.72. They reported the average annual direct cost per AS patient as €3565.91. The majority of these direct costs are attributed to medication, which accounts for 97.1% of the total direct expenses. Other

direct costs include diagnostic tests (1.2%), outpatient visits (0.8%), physiotherapy (0.5%), consultations (0.3%), and hospital care (0%). These findings are comparable to the results of the current study. The average annual indirect cost due to productivity losses per AS patient, calculated using the Human Capital Approach, is €6989.81. This breakdown includes €245.50 for lost working days, €31.38 for sick leave, €2805.39 for early retirement, €374.05 for early death, and €3533.67 for disability. In the current study, the loss of productivity amounted to €1059.60, and the cost of lost workdays was €313.40. The main contributor to indirect costs in the current study is the loss of productivity, highlighting the significant economic impact of chronic conditions like AS. Although the cost associated with early retirement and work disability is relatively low (€122.60), it still represents a crucial aspect of the disease's impact, reflecting a smaller but significant portion of the overall economic burden.

In the current study, the patients were grouped according to the BASDAI scores, and the costs were compared between the groups. The costs of medications and the total direct costs were determined to be higher in the group with a BASDAI score <4 ($P = .039$). This could have been because the cost of anti-TNF drugs comprised 99.6% of the total medication costs, and while 74.3% of the patients in the BASDAI ≥4 group were using anti-TNF, it was used by 90.8% of the patients with a BASDAI score <4.

In the current study, we based the sample size on the average number reported in the systematic review by Rudwaleit et al,[29] which included 11 studies with sample sizes ranging from 103 to 334. The sample size calculation was performed with a 95% confidence interval and a 5% margin of error. Considering that the prevalence of AS in our country is 0.46%,[30] a sample size of 100 provides a reasonable estimate of the direct and indirect costs. However, this sample size results in wider confidence intervals, and the study's findings may not be fully generalizable to the entire Turkish population. Future research with a larger, multi-center sample would be beneficial for enhancing the generalizability of the results and providing more precise estimates.

The main limitation of this study was that the cross-sectional design did not allow for the examination of the predictive value of AS-WIS for work disability. Psychosocial factors (fear of return to work, work-related stress, job satisfaction) that could be predictive for work-related outcomes could not be evaluated. No relationship could be proven between work instability and anti-TNF treatment. This could be due to patients having a long disease duration and possibly more severe disease. The effect of TNF blockers on work instability has not been determined as yet. If future studies confirm the effect of anti-TNF treatment on work instability, part of the cost of these treatments could be balanced by a reduction in the economic costs related to work loss.

The results of this study demonstrated that in conditions of active disease, there is an increase in absenteeism, presenteeism, and overall work impairment. In addition to healthcare costs, the costs related to unemployment, absenteeism, and loss of work productivity comprise a significant proportion of the total costs. Therefore, it seems very important for AS patients to achieve an inactive disease status and thereby maximize job retention.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of Akdeniz University, (Approval no.: 70904504/626, Date: October 04, 2021).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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