Turkish Journal of Diabetes and Obesity / *Türkiye Diyabet ve Obezite Dergisi*
Original Article / Özgün Araştırma

The Effect of Obesity in Individuals with Ankylosing Spondylitis: A Single Center Cohort Study

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Cite this article as: Gur Kabul E et al. The effect of obesity in individuals with ankylosing spondylitis: a single center cohort study. Turk J Diab Obes 2024;1: 43-50.

ABSTRACT

Aim: The aim of this study was to compare the disease activity and functional status of individuals with Ankylosing Spondylitis (AS) according to body mass index (BMI).

Material and Methods: This study, which was planned as a single-center cohort study, included 437 individuals with AS. Disease activities were evaluated with the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and functional levels with the Bath Ankylosing Spondylitis Functional Index (BASFI). Participants were categorized in 3 groups according to BMI data based on the criteria of the World Health Organization: normal weight:20-24.9; overweight: 25-29.9; obese:≥30. One Way Anova Test, Kruskal Wallis Test, Mann Whitney U test and Chi-Square Test were used to compare independent group differences. Linear regression models were used to describe the relationship between BASDAI, BASFI (dependent variables) and BMI categories (independent variables). Univariate regression analyses were performed (only one independent variable in the model).

Results: Among 437 patients with AS, 30.2% are normal weight, 39.5% are overweight and 30.2% are obese. Analysis results of data between BMI groups; significant difference was in BASFI (p=0.001) in favor of the obese group. In binary group comparisons for BASFI; there was a significant difference in favor of the obese group between normal and obese (p=0.002) and between overweight and obese (p=0.001). Obese was significantly associated with higher BASFI score compared to the normal weight group without adjustment for covariates (β:-0.37, 95%CI -0.66/-0.08, p=0.006). On the other hand, there was no association between BASDAI and obesity (β:-0.50, 95%CI -1.11/ 1.22, p:0.130).

Conclusion: The BMI of Turkish AS individuals in a single center cohort had no effect on disease activity, but obesity had a worse effect on functional level.

Keywords: *Ankylosing spondylitis, Body mass index, Overweight, Disease*

Ankilozan Spondilitli Bireylerde Obezitenin Etkisi: Tek Merkezli Kohort Çalışması

ÖZ

Amaç: Bu çalışmanın amacı Ankilozan Spondilitli (AS) bireylerin hastalık aktivitesini ve fonksiyonel durumlarını vücut kütle indeksine (VKİ) göre karşılaştırmaktır.

Gereç ve Yöntemler: Tek merkezli kohort çalışması olarak planlanan bu çalışmaya, AS tanılı 437 birey dahil edildi. Hastalık aktiviteleri Bath Ankilozan Spondilit Hastalık Aktivite İndeksi (BASDAI), fonksiyonel düzeyleri ise Bath Ankilozan Spondilit Fonksiyonel İndeksi (BASFI) ile değerlendirildi. Katılımcılar, Dünya Sağlık Örgütü'nün kriterlerine dayanarak VKİ verilerine göre 3 gruba ayrıldı: normal ağırlık:20-24,9; fazla kilolu: 25-29,9; obez:≥30. Bağımsız grup farklılıklarının karşılaştırılmasında One Way Anova Testi, Kruskal

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DOI: 10.25048/tudod.1450923

Received / *Geliş tarihi* : 11.03.2024
Revision / *Revizyon tarihi* : 15.04.2024
Accepted / *Kabul tarihi* : 17.04.2024

Wallis Testi, Mann Whitney U testi ve Ki-Kare Testi kullanıldı. BASDAI, BASFI (bağımlı değişkenler) ve VKİ kategorileri (bağımsız değişkenler) arasındaki ilişkiyi tanımlamak için doğrusal regresyon modelleri kullanıldı. Tek değişkenli regresyon analizleri yapıldı (modelde yalnızca bir bağımsız değişken).

Bulgular: AS'li 437 hastanın % 30.2'i normal ağırlıkta, %39,5'i fazla kilolu, %30,2'i ise obezdir.

UKİ grupları arasındaki verilerin analiz sonuçlarında; BASFI'de (p=0,001) obez grup lehine anlamlı fark vardı. BASFI için ikili grup karşılaştırmalarında; normal ile obez (p=0,002) ve fazla kilolu ile obez (p=0,001) arasında obez grup lehine anlamlı fark vardı. Ortak değişkenler için düzeltme yapılmadan normal ağırlıklı grupla karşılaştırıldıklarında, obezite daha yüksek BASFI skoru ile anlamlı düzeyde ilişkiliydi (β:-0,37, %95CI -0,66/-0,08, p=0,006). Öte yandan, BASDAI ile obezite arasında herhangi bir ilişki yoktu (β:-0,50, 95%CI -1,11/ 1,22, p:0,130).

Sonuç: Tek merkezli bir kohorttaki, Türk AS'li bireylerin VKİ'nin hastalık aktivitesi üzerine etkisi yoktu, ancak obezite fonksiyonel düzey üzerinde daha kötü bir etkiye sahip idi.

Anahtar Sözcükler: *Ankilozan spondilit, Vücut kütle indeksi, Fazla kilo, Hastalık*

INTRODUCTION

Cardiovascular (CV) problems are among the most important and notable causes of death in the world. Many studies have emphasized that CV events and mortality are increased in individuals with Ankylosing Spondylitis (AS). One of the traditional cardiovascular risk factors is obesity (1-3). Globally, obesity has been on the rise since 1980. This increase is more than doubled. Obesity is an abnormally high amount of fat in the body. The World Health Organization defines it this way (4).

The most commonly used measure for estimating body fat percentage is Body Mass Index (BMI). World Health Organisation (WHO) also recommends BMI as the most useful population level measure of overweight and obesity (5,6). BMI is a recently widely used metric calculated with height and weight data, which are anthropometric characteristics in the adult population and both sexes. It is possible to categorize these data into groups. BMI equal to or greater than 25 is called overweight, and BMI equal to or greater than 30 is called obese (4).

Obesity is actually among the modifiable cardiovascular risk factors. Although there is a lot of information in the literature about its importance, there are not enough studies that can clarify whether there is a difference in clinical outcomes in overweight and obese AS patients with high BMI compared to normal weight patients. A recent systematic review and meta-analysis reported that more studies are needed to elucidate whether the increase in BMI generally contributes to disease activity in axial spondyloarthritis (7).

This study was planned to compare the activity and functional status of individuals with AS categorized according to BMI data.

MATERIALS and METHODS

Study Design

This study was planned as a single center cohort study. Between November 2021 and February 2022, patients who applied to the Pamukkale University Rheumatology clinic and the registered patients who were contacted by phone and agreed to participate in the study constituted the sample of the study. Pamukkale University is a centre in Turkey. Patients were given appointments and evaluated.

Participants

437 patients with AS diagnosed by a rheumatologist included.

Inclusion criteria: (a) being diagnosed with AS according to the modified New York criteria. (b) volunteer to participate. (c) be in the age range of 18-65 years. Exclusion criteria: (a) neurological, cardiopulmonary, and/or orthopedic disease (b) cognitive disability that is unable to cooperate. (c) being pregnant. (d) presence of other autoimmune or inflammatory disease. (e) central nervous system diseases (f) serious psychiatric conditions (g) any surgical operation in the last six months. (h) BMI <20.

According to the Helsinki Declaration of 1975, as revised in 1983, it was determined at the meeting held by the local ethical committee that there was no ethical problem for the study to be carried out (decision no: 21, dated: 11.30.2021). All patients were informed verbally and informed consent forms were signed.

Evaluations

After the demographic information was recorded, disease activities were evaluated with the Bath Ankylosing Spondylitis Disease Activity Index, and functional levels with the

Bath Ankylosing Spondylitis Functional Index. Participants were categorized in 3 groups according to BMI data based on the criteria of the World Health Organization: normal weight:20-24.9; overweight: 25-29.9; obese:≥30 (4). Evaluations were carried out in approximately 25 minutes.

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI): With this index, the disease activity level can be easily evaluated with 6 questions (weakness/fatigue level, spine pain level, the level of pain in the joints other than the spine, sensitivity level, morning stiffness duration, morning stiffness severity). It was proven to be valid and reliable with its sensitivity and reproducibility features. The total score of BASDAI was calculated by the sum of questions 1-4 plus mean of questions 5 and 6, the total then divided by 5. The total score ranges from 0 to 10, higher values indicate more active disease (8).

Bath Ankylosing Spondylitis Functional Index (BASFI): The level of being able to perform the activities that are frequently done in daily life is determined with 10 questions. The patient thinks about the past week and answers the questions. For each question, patients mark on the 10 cm Visual Analog Scale (VAS) how difficult they are while doing the activity (0=easy, 10=impossible). A total score is calculated by averaging the score obtained from 10 questions (from 0 to 10) (9).

Statistical Analysis

The data were analyzed using IBM Statistical Package for the Social Sciences (SPSS) Statistics vn.22 software. The Kolmogorov-Smirnov test was performed to ensure that the data conformed to the normal distribution. Categorical descriptive data were written as numbers and percentage, while continuous descriptive data were written as mean±SD or median (minimum-maximum) according to fit for normal distribution. One Way Anova Test, Kruskal Wallis Test, Mann Whitney U test and Chi-Square Test were used to compare independent group differences. Linear regression models were used to describe the relationship between BASDAI, BASFI (dependent variables) and BMI categories (independent variables). Univariate regression analyses were performed (only one independent variable in the model). Statistical significance value was $p<0.05$.

RESULTS

Participant Flow

The study was first started with 508 patients with AS. Twelve patients with AS did not want to participate in the study. Fifty seven patients with AS had other autoimmune or inflammatory disease. Two patients with AS had surgical operation in the last six months. Consequently, the study was completed with a total of 437 patients with AS (247 female, 190 male) with a mean age of 42.4±10.8 years. The flow chart of the study is shown in Figure 1.

Recruitment

The dates determining the recruitment periods were November 2021- February 2022.

Baseline Data

The demographic data of the participants are shown in Table 1.

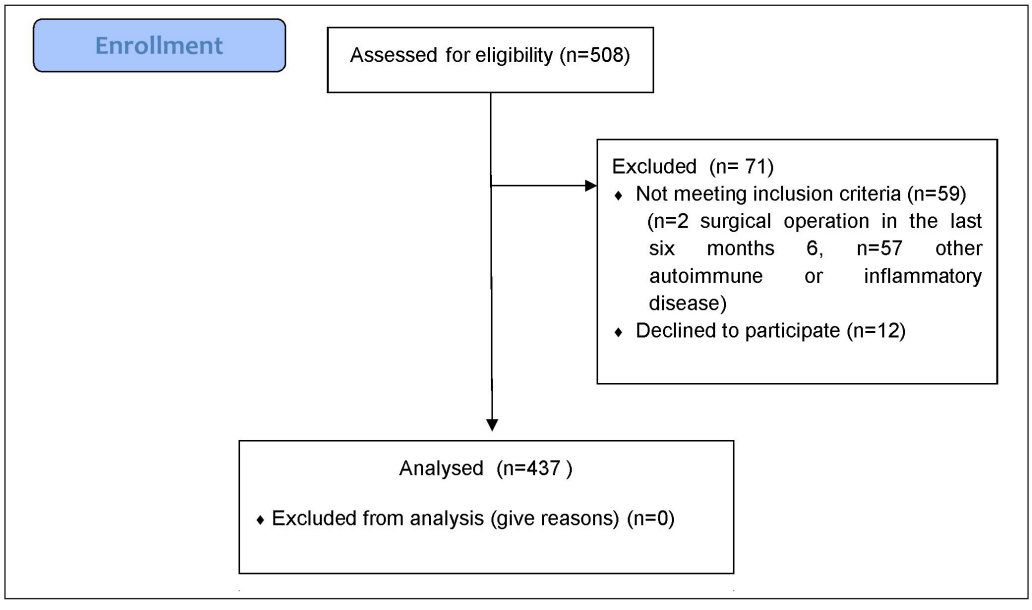

Figure 1: The flow chart of the study.

Table 1: The demographic data of the participants

Variables, n(%)		Ankylosing Spondylitis (n=456)			
		Normal Weight <25 kg/m² (n=132)	Overweight 25<n<30 kg/m² (n=173)	Obese ≥30 kg/m² (n=132)	p
BMI		132 (30.2)	173 (39.5)	132 (30.2)	
Gender	Female	66 (50)	88 (50.9)	93 (70.5)	0.001*
	Male	66 (50)	85 (49.1)	39 (29.5)	
Employed	Yes	72 (61)	95 (62.5)	51 (39.8)	0.001*
	No	46 (39)	57 (37.5)	77 (60.2)	
Family history for rheumatic diseases	Yes	33 (32.7)	72 (51.8)	44 (37.9)	0.007*
	No	68 (67.3)	67 (48.2)	72 (62.1)	
Smoker	Yes	35 (31)	55 (37.7)	24 (20.2)	0.008*
	No	78 (69)	91 (62.3)	95 (79.8)	
History of chronic respiratory disease	Yes	11 (11)	19 (14.7)	28 (27.2)	0.006*
	No	89 (89)	110 (85.3)	75 (72.8)	
Physical exercise habits	Yes	28 (29.5)	29 (24.4)	20 (20.6)	0.361*
	No	67 (70.5)	90 (75.6)	77 (79.4)	
		Mean ± SD	Mean ± SD	Mean ± SD	
Age (years)		37.6±11.2	42.7±10.1	46.7±9.4	0.001***
		Median (Min/Max)	**Median (Min/Max)**	**Median (Min/Max)**	
Duration of the disease (years)		6 (0/40)	6 (0/32)	6 (0/33)	0.540**
Years of education		8 (1/21)	8 (1/16)	5 (2/18)	0.141**
Back stiffness in the morning (minutes)		20 (0/240)	15 (0/240)	15 (0/240)	0.363**

*Chi-Square Test, **Kruskal-Wallis Test, *** One Way Anova Test

Table 2: Analysis results of outcome measures data between BMI groups

	BASFI (n=437)	BASDAI (n=437)
	Median (min/max)	**Mean±SD**
Normal Weight (n=132)	2.2(0/10.8)	4.1±2.0
Overweight (n=173)	2.6(0/9)	4.2±2.2
Obese (n=132)	3.8(0/18.7)	4.6±2.0
Normal-overweight-obese, p	0.001*	0.104***
Normal-overweight, p	0.939**	
Normal-obese, p	0.002**	
Overweight-obese, p	0.001**	

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, **BASFI:** Bath Ankylosing Spondylitis Functional Index, *Kruskal-Wallis Test,** Mann Whitney U Test,*** One Way Anova Test

Compared with the normal and overweight groups, the obese group had the highest proportion with female (normal=50%, overweight=50.9%, obese=70.5%; p=0.001); had the lowest proportion with employed (normal=61%, overweight=62.5%, obese=39.8%; p=0.001); had the greatest percentage with history of chronic respiratory disease (normal=11%, overweight=14.7%, obese=27.2%; p:0.006); was older (normal=37.6±11.2 years, overweight=42.7±10.1 years, obese=46.7±9.4 years; p=0.001). Compared with the normal and obese groups, the overweight group had the highest proportion with family history for rheumatic diseases (normal=32.7%, overweight=51.8%, obese=37.9%; p=0.007) and with smoker (normal=31%, overweight=37.7%, obese=20.2%; p=0.008). Although there is no difference between the three groups in terms of physical exercise habits, it is seen that the percentages of "no" answers to physical exercise habits are high in all three groups (Table 1).

Outcome Measures

Analysis results of data between BMI groups; significant difference was in BASFI (p=0.001) in favor of the obese group. In binary group comparisons for BASFI; there was a significant difference in favor of the obese group between normal and obese (p=0.002) and between overweight and obese (p=0.001) (Table 2).

Table 3: Univariate analysis of association between outcome measures variables and BMI groups

Dependent variable	Predicting variable	Univariate analysis, β (95%CI)	p value
BASDAI	Overweight[h]	-0.06(-0.64/0.51)	0.960
	Obese[h]	-0.50(-1.11/0.10)	0.130
BASFI	Overweight[h]	0.04(-0.22/0.31)	0.915
	Obese[h]	-0.37(-0.66/-0.08)	0.006

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, **BASFI:** Bath Ankylosing Spondylitis Functional Index, [h]Reference group: Normal weight

Univariate Analysis

In Table 3, obese was significantly associated with higher BASFI score (β -0.37, 95% CI -0.66, -0.08) compared to the normal weight group without adjustment for covariates.

DISCUSSION

In this study, the effect of BMI on disease activity and functional level was investigated in a cohort of Turkish AS individuals who received treatment from a center in Turkey. As a result, while 39.5% of the cohort was overweight, 30.2% were obese, and BMI had no effect on disease activity, it was determined that the functional level was worse in the obese group.

Obesity, which has become epidemic today, is a big problem in the field of health: Due to the increase in body fat, it creates many problems for general health, seriously reduces the quality of life and prevents the prolongation of life expectancy. The high prevalence of obesity in AS is of particular concern in this group, which is largely attributed to accelerated cardiovascular risk (10,11). BMI is considered a good predictor of body fat. It can be easily measured and is a good indicator for estimating disease risk (12).

The results of studies examining the relationship between BMI and patient-reported outcomes in an AS population in one country may not be valid for populations of another country (13). Since most of the findings in the literature on the relationship between AS and BMI were obtained as a result of studies carried out in Europe, the generalizability of these data belonging to a limited geographical area is limited (7).

In the literature, there are different results regarding the relationship between patient-reported outcomes and obesity in patients with AS categorized according to BMI. Despite the studies conducted, it is still unclear whether high BMI is associated with higher disease activity in axial spondyloarthritis (axSpA), further studies are needed in this regard (7).

Lee et al. stated that 32% of 194 axSpA in an urban Asian population were overweight while 22% were obese. They concluded that while obesity was associated with pain, BASDAI, BASFI, Health Assessment Questionnaire, and Short Form-36 were not, and that future studies examining the causal relationship between obesity and patient-reported outcomes are needed (13). In a study by Durcan et al., 67.5% of 46 patients in AS Ireland Population were overweight or obese. There was a statistical difference in BASFI and BASDAI between normal and overweight AS patients (14). In the study of Berg et al. with 159 AS patients in the norway population, they reported in the regression analysis that the BMI-high group had higher Ankylosing Spondylitis Disease Activity Score (ASDAS) and BASDAI, increased cardiovascular disease risk factors and increased carotid intima media thickness than the BMI-low group. Therefore, they stated that obesity may be a factor for increased disease activity and increased cardiovascular disease risk (15).

In the study of Maas et al. with 461 patients axSpA in Netherlands, overweight and obese were 37% and 22%, respectively. Compared to the general population, obesity was more common in people with axSpA. In axSpA, when compared to overweight and normal weight patients, the clinical picture (disease activity, quality of life and physical function) of obese patients was much worse and their symptoms lasted much longer with more comorbidities (16). In a study conducted in Ireland with 683 axSpA patients; underweight, normal, overweight, obese were 1.1; 31.6; 38.9; 28.4%, respectively. Total overweight or obese were 67.3% with longer disease duration and more comorbidities than normal weight patients. Obese patients have significantly worse the clinical picture (disease activity, spine mobility, quality of life and physical function) than normal and overweight. Higher BMI and obesity independently predict worse disease course. Strategies should be implemented to control BMI and reduce it to normal levels in axSpA (17). In a study conducted with 509 Norwegian patients, normal/underweight and overweight/obese were 35% and 65%, respectively. The conclusion was emphasized that BMI should be considered in the treatment of Norwegian overweight/obese axSpA patients due to the higher number of disease activity, spinal stiffness and comorbidities (18).

In a systematic review and meta-analysis by Jean et al, it was stated that as the BMI increases, the disease activity increases due to the increase in the amount of fat in the body and this makes it difficult for patients to cope with the disease (7). In a study of Vargas et al. with 683 patients in european (multicenter) population; 26.4% were overweight and 13.3% obese. The authors stated that ASDAS and BMI are not related in axSpA patients based on the data. It is unnecessary to consider BMI in treatment (19).

To authors' knowledge; there is only one study investigating the effect of BMI on patients with AS in the Turkish population. In this study, in which 28 patients with pre-obese AS (BMI in range of 25 to 30) were evaluated, a relationship was determined between BMI and BASDAI and BASFI. It has been reported that increased BMI in patients with AS is a factor affecting clinical picture (quality of life, functional capacity and disease activity) (20).

According to the results of this study, 39.5% of AS patients were overweight, 30.2% were obese. In this study, the BASFI scores of the obese AS patients were worse, but there was no statistical difference between the groups for BASDAI. When the authors' of the present study look at the above studies reporting that there is a relationship between disease activity and obesity, the disease duration is longer than in the present study population and this finding may affect this relationship. Additionally, the mean age in these studies is also higher. In the present study, the authors attribute BMI had no effect on disease activity to lower disease duration and lower mean age. More than that, the obese AS group of the present study was more females. van der Slik et al. reported that female experienced significantly worse physical function and quality of life, whereas male showed significantly more kyphosis and spinal radiographic damage (21). Falkenbach et al. emphasized that there is a significant difference in the BASFI score between younger and older patients with AS. Older patients with AS had worse scores (22). In addition, many studies in the literature were stated that obese AS patients were older compared with the normal and overweight groups (7,13,16). The reason for the significant difference in BASFI and no difference in BASDAI was thought to be gender, disease activity and age distribution. For this reason, the authors of the present study recommend the evaluation of obesity, especially in female, older and longer disease duration patients with AS. However, there are many factors that will affect disease activity, such as cytokine level, age of onset of the disease, pain level and inflammatory markers in the blood, so the effect of these factors can be examined together in future studies.

Physical activity improves spinal mobility, physical functionality, the general condition of the patient and reduces pain; therefore recommended in AS but poorly performed (23). One of the reasons for low activity level may be pain. Low activity level can lead to obesity. Obesity increases the weight on the joints (24). Obese people feel more pain because excess body mass causes mechanical stress and an increase in proinflammatory cytokines (25). Pain is one of the most important factors leading to an inactive life and can pull the person into an endless cycle (26). This makes the disease worse. In the present study cohort, exercise habits are at low levels in all three groups categorized according to BMI. The authors of the present study thought that the obese AS patients in the cohort are in this vicious circle and therefore worse functional level scores were observed in the obese group.

In AS patients, exercise has a very important place in the management of the disease, disease-specific variables (better spinal mobility, maintenance of functional capacity and reduced pain and stiffness) and in controlling the risks (14,27,28). For this reason, the authors of the present study believe that exercise therapy, which will provide weight loss, especially in obese AS patients, will contribute to increasing the well-being of the disease.

One of the limitations of the present study is that it does not allow us to make inferences about the causal relationship between patient-reported outcomes and obesity due to its cross-sectional design. Future prospective studies are needed to determine this causal relationship.

The strength of the present study is the prevalence of overweight and obesity has been evaluated for the first time in a large cohort of AS patients from the Turkish population.

As a result of this study, clinicians, researchers and patients should take into account the possible beneficial effects of weight within the normal range for better management as functional limitation is observed to be more in obese Turkish patients with AS.

Conflicts of interest
The authors declare that there is no conflict of interest.

Ethical approval
Approval for the study was granted by the Ethics Committee of Pamukkale University (decision no: 21, dated: 11.30.2021). All individuals were informed verbally and informed consent forms were signed. This study was conducted in accordance with the Declaration of Helsinki.

Funding
The authors declared that this study had received no financial support.

Acknowledgments
None.

Author contributions
Design of the study: **Elif Gur Kabul, Bilge Basakci Calik,** Data acquisition: **Elif Gur Kabul, Bilge Basakci Calik, Sinem Kuru,** Eligibility for inclusion criteria and diagnosis: **Murat Yigit, Veli Cobankara,** Data analyses, interpretation of the results and write the manuscript: **Elif Gur Kabul,** The critical revision of the manuscript for the final version: **Bilge Basakci Calik, Veli Cobankara.**

Peer Review Process
Extremely and externally peer-reviewed.

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