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The Relationship of Body Mass Index with Disease Activity in Ankylosing Spondylitis

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ABSTRACT

Find out the relationship between body mass index (BMI) and W.C with disease activity score in AS patients and its association with clinical characteristics of AS. One hundred and five patients (75 male and 30 female) who visited rheumatology and medical rehabilitation center in Sulaimani city were recorded in this cross-sectional study. Disease activity was measured by ASDAS-ESR in the hand-held calculator. BMI was calculated and waist circumference (W.C.) was measured and both were evaluated with disease activity score and disease characteristics in those with normal BMI and W.C and those with abnormal BMI and W.C. Data of one hundred and five patients were involved in this study with a mean age of 37±9.5 years with the predominance of male gender (71.4%). The mean BMI of the patients was 27.2±4.6 kg/m², 28.6% of them were obese and 35.2% of them were overweight. Patients who were overweight, obese and increased W.C had significantly higher disease activity scores and older compared to those who had normal BMI and W.C(p value<0.05).There was no statistically significant difference between the two groups in terms of peripheral arthritis, disease duration, clinical characteristics of AS, and gender (P value>0.05). Overweight, obesity and increased W.C are common among AS patients and significantly related to disease activity score and age, but not with disease characteristics and gender.

Keywords;**Ankylosing.spondylitis.Obesity.BMI.Disease activity**

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علاقة مؤشر كتلة الجسم مع نشاط المرض لدى مرضى التهاب الفقار اللاصق

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الملخص

معرفة العلاقة بين مؤشر كتلة الجسم (BMI) ، ومحيط الخصرمع درجة نشاط المرض لدى مرضى AS وعلاقتها ببعض الخصائص الديموغرافية والسريرية لـ AS. مائة وخمسة مرضى (75 ذكور و 30 أنثى) الذين زاروا المستشفى التعليمي العام /قسم المفاصل والتاهيل الطبي في السليمانية ، المسجلين في هذه الدراسة المستعرضة. تم قياس نشاط المرض باستخدام آلة حاسبة .تم حساب مؤشر كتلة الجسم ومحيط الخصر (WC) وحساب علاقتهما مع درجة نشاط المرض (ASDAS–ESR) وبعض خصائص المرض لدى أولئك الذين يعانون من مؤشر كتلة الجسم الطبيعي وأولئك الذين يعانون من السمنة المفرطة والوزن الزائد، تم تحليل النتائج إحصائيا. تم تقييم ما مجموعه 105 مريضا في هذه الدراسة مع متوسط العمر (37 ± 9.5)سنوات مع هيمنة الجنس من الذكور (71.4 ٪). كان متوسط مؤشر كتلة الجسم للمرضى(27.2 ± 4.6)كجم / م² ، 28.6٪ منهم يعانون من السمنة المفرطة و 35.2 ٪ منهم يعانون من زيادة الوزن. كانت هناك فروق ذات دلالة إحصائية بين أولئك الذين كانوا يعانون من زيادة الوزن ، والسمنة و wc غير طبيعية والذين لديهم مؤشر كتلة الجسم العادي و wc الطبيعي فيما يتعلق بدرجة نشاط المرض المقاسة ASDAS–ESR والعمر (P <0.05). لم تكن هناك فروق ذات دلالة إحصائية بين المجموعتين من حيث التهاب المفاصل المحيطي ، ومدة المرض ، والخصائص السريرية لل AS ، والجنس (P> 0.05). فرط الوزن ,السمنة و زيادة محيط الخصرشائع بين مرضى التهاب الفقار اللاصق ويرتبط بدرجة كبيرة بنتيجة نشاط المرض ، ولكن ليس مع خصائص المرض والجنس.

الكلمات الدالة: التهاب الفقار اللاصق. بدانة؛ مؤشر كتلة الجسم؛محيط الخصرو نشاط المرض

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1. Introduction

Ankylosing spondylitis (AS) is a chronic, inflammatory disease that affects the sacroiliac joints and the spine and manifests with pain, joint stiffness, and loss of spinal mobility [1]. However, many patients have extra spinal manifestations such as arthritis, enthesitis and ductility's, and extra-articular manifestations, such as uveitis, psoriasis and inflammatory bowel disease (IBD) [2] .AS makes part of the seronegative spondyloarthropathies (SPA) .SPA represents a group of inflammatory arthritis diseases which share some clinical, genetic, and immunologic features [3]. Male are more often affected than females, with a ratio of 3:1 [4].

The prevalence of AS in different populations varies from 0.1 in African and Eskimo populations , 0.5 % to 1 % in the United Kingdom and the United States, to around 6% in the Haida Native Americans in Northern Canada [5]. It has been evaluated that about 90% of the pathogenesis of AS is genetically determined. [6]. HLAB27 gene is strongly linked with AS ; 90–95% of patients with AS are positive for HLA-B27 [7].The chance of developing AS if one is HLA-B27 positive is 1-5%, reach to 15-20% for people with an affected first degree of a family member [8]. An environmental factor triggers AS in an individual who is genetically predisposed [9].

The clinical manifestations of AS usually commence in early adulthood or late adolescence, with arrival after the age of 45 is unusual [10].There is no diagnostic laboratory study in AS.

The studies of Hematology are usually normal. The erythrocyte sedimentation rate and C-reactive protein are elevated in more than half of cases and tend to be associated with peripheral disease activity [11]. The diagnosis of AS is based on a combination of symptoms, physical findings and imaging studies establish the AS. In the absence of specific diagnostic manifestation. we rely on classification criteria. The modified New York Criteria is one of the most widely used classification criteria for AS [12]. Disease activity concept is a reflection of the underlying inflammation, includes a wide range of domains and measures [13].The most frequently used instrument for disease activity is BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) [14]. Moreover, it is not sensitive to change [15] and does not include objective activity measures [16]. The new composite index to assess disease activity in AS is the ASDAS which is short for (Ankylosing Spondylitis Disease Activity Score) [17]..The ASDAS containing Erythrocyte Sedimentation Rate (ESR in mm/h) is selected as a disease activity measure. The 4 additional self-report items included in this index, aside from the value of ESR, are back pain [visual analog scale (VAS) 0–10 cm, or numerical rating

scale (NRS) 0–10], duration of morning stiffness (VAS/NRS), peripheral pain/swelling (VAS/NRS), and patient global assessment of disease activity (VAS/NRS ;) [17, 18].

The ASAS members discussed and nominated to define 4 disease activity states: inactive disease (<1.3), moderate disease activity (1.3 to <2.1), high disease activity (2.1 to 3.5), and very high disease activity (>3.5 score) [19].

AS patients like patients with other rheumatic diseases that are included rheumatoid arthritis, having an increased risk of metabolic syndrome when compared to the general population [20, 21].. Adipokines dysregulation, which are bioactive substances that are secreted by adipocytes and immune cells occur in individuals that suffer metabolic syndrome [22, 23].

A change in body composition is caused by muscle weakness, decreased muscle function and physical inactivity in AS. Quantity of lean tissue is reduced in AS, which makes total fatty tissue more conspicuous [24]. In AS, the role of excess adipose tissue has not been studied widely, the link between excess adipose tissue and inflammation in AS is suggested by some indirect results [25]. An increase in adipose tissue, which is regarded to be a dynamic endocrine organ, is related to increased production of pro-inflammatory cytokines, coagulation mediators, complement factors, IL1, and TNF [26, 27]. Low-grade inflammation of obese subjects is resulted from the overproduction of adipokines with pro-inflammatory properties and thus contributes to the expansion of metabolic disturbances and intensification of inflammatory responses [28].

2.Patients and Methods

In this cross-sectional study, a total of 105 patients (75 male&30 females) were enrolled. Diagnosis of patients was made according to the modified New York criteria from those who visited the division of rheumatology in an internal medical teaching hospital in Sulaimani .from May to November 2018

The exclusion criteria were other chronic or autoimmune inflammatory arthritis, infection, .CNS disorders, drug and alcoholic abuse

The demographic data of the patients including age, weight, height, BMI (BMI= Weight/Height^2, Kg/m^2), Waist circumference (W.C, cm), sex, disease duration, enthesitis, and peripheral joint involvement, were noted through direct interview and fulfilling the .prepared questionnaire

According to patients' BMI, their BMI was organized into 3 categories: normal BMI ≤24.9 kg/m², overweight 25.0 -29.9 kg/m², and obesity that was considered with BMI ≥30 kg/m² [29].Waist Circumference (W.C) is measured with a tape, the subject standing, at the level midway between the lower rib margin and iliac crest [30].Because the measurement of the visceral fat component is costly; therefore, W.C is used as a marker of abdominal fat mass. W.C cutoffs are (W.C < 80 cm for females and < 94 for males) for those who were not at increased risk of comorbidity, (W.C ≥ 80 cm for females and ≥94 cm for males) for those who were at increased risk of comorbidity [31] Evaluation of disease activity was done by using ASDAS-ESR (ESR, mm/hr), which was measured by hand-held calculator. All patients' data entered using computerized statistical software; Minitab 18 was used. Descriptive statistics are presented as (mean± standard deviation) and frequencies as percentages. Chi-square, and Kruskal Wallis tests were utilized as appropriate to analyze the relationship between BMI categories and patient characteristics and clinical outcomes in a patient with AS. Statistical significance was set as p-value of less than 0.05.

3.Results and Calculations

About one hundred and five AS patients were involved in the present study with the age of 37±9.5 years, 21 %(22) of them were aging 20-29 years. The higher percentages 39 %(41) were for those with age group 30-39 years. Males were more than females with a ratio as 2.5:1. The mean BMI of patients was 27.25±4.6 kg/m², obese patients were about 28.6 %(30), and overweight was 35.2 %(37) and 36.2 %(38) for patients with normal BMI. Mean waist circumference (W.C) of patients was 100±11.2 cm, 31.4 %(33) of them were with normal W.C, while 68.6 %(72) of them with W.C higher than normal (increased risk of comorbidity). The percentage of patients with a disease duration of ≤ 5 years was 41.9 %(44). Thirty nine of patients were presented with peripheral arthritis, while 58 had extraarticular manifestations, 44 had enthesitis and 14 had uveitis. The mean ESR of patients was 22±22.1 mm/hr, 50 (47.6%) of AS patients had high ESR.

Mean ASDAS-ESR of studied patients was (2.4±1.0), 17(16.2%) was inactive, 25(23.8%) of the patients had moderate disease activity, 44(41.9%) had high disease activity and19 (18.1%) had very high disease activity. Table 1

Table 1: characteristics of patients

Characteristics	Total(n=105)
Age(year)	37.25±9.5
20-29	22(21%)
30-39	41(39%)
40-49	33(31.4%)
≥50	9(8.6%)
Gender	
Male	75
BMI(kg/m²	27.25±4.6
normal	38(36.2%)
overweight	37(35.2%)
obese	30(28.6%)
W.C(cm)	100±11.19
normal	33(31.4%)
increased W.C	72(68.6%)
Disease duration(mean,SD)	8.19±6.78
≤5 years	44(41.9%)
Peripheral arthritis	39(37.1%)
Uveitis	14(13.3%)
Enthesitis	44(41.9%)
ESR(mm/hr)	22.02±22.16
ASDAS-ESR	2.46±1.01
Inactive	17(16.2%)
Moderate disease activity	25(23.8%)
High	44(41.9%)
Very high	19(18.1%)

ASDAS-ESR was higher in the overweight and obese category compared with those with normal weight category and this was statistically noteworthy (p-value < 0.05).

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The older patients that were overweight and obese, had a longer disease duration; these results were statically significant only for age (p value of less than 0.05) as presented in Table 2.

Table 2: Distribution of disease activity age, and disease duration according to BMI of AS patients

Variable	BMI			P-value
	Normal N=38	Overweight N=37	Obese N=30	
ASDAS	2.3±1.0	2.41±1.04	2.8±0.92	0.01
Age	32.6±7.84	39.27±9.15	40.64±10.1	0.001
Disease duration	6.92±5.7	9.16±6.7	8.6±8.16	0.29

No substantial differences were perceived between AS patients with normal BMI and those with overweight and obese regarding clinical symptoms and gender (p value of less than 0.05) as presented in Table 3.

Table 3 Distribution of peripheral arthritis, extra particular manifestations and gender according to BMI

Variable	BMI			Total	P-value
	Normal N=30	Overweight N=37	Obese N=30		
Peripheral arthritis					
Yes	12	14	13	39	0.6
No	26	23	17	66	
Uveitis					
Yes	8	4	2	14	0.17
No	30	35	28	91	
Enthesitis					
Yes	11	14	15	44	0.09
No	26	23	15	61	

Gender					
Male	28	26	21	75	0.93
Female	10	11	9	30	

AS patients with waist circumference higher than normal were had higher disease activity and older in age compared with those with normal waist circumference and these results were statistically significant (p value of less than 0.05), no significant differences was witnessed between the two groups regarding disease duration (p value greater than 0.05) as presented in Table 4

Table 4 Disease activity, age, and disease duration according to waist circumference

Variable	Waist Circumference		P-value
	Normal N=33	Increased Risk N=72	
ASDAS-ESR	2.07±1	2.67±1	0.007
Age (years)	32±7.2	40±9.5	< 0.001
disease duration (years)	6.97±5.69	8.8±7.68	0.23

4.Conclusion

Overweight, obesity and increased W.C are common among AS patients and significantly .related to disease activity score and age

No significant association had been seen between BMI, some clinical manifestation of AS (peripheral arthritis, uveitis and enthesitis), and gender. Additional longitudinal studies are vital to know the effect of obesity on AS pathophysiology and more studies are required to detect and monitor the response of the disease in normal and obese patients to different types of treatment.

4.Discussion

AS is a seronegative chronic inflammatory disease that involves the sacroiliac joints and the axial skeleton. Back pain and progressive stiffness of the spine characterized the AS. Arthritis of the hips and shoulders, enthesitis, and anterior uveitis are common. [32]

Obesity and overweight are increasing universally and now approach a third of the world population [33]. The World Health Organization (WHO) defines obesity as an abnormal or excessive fat accumulation that presents a risk to health [34].In AS the role of excess adipose tissue has not been studied widely; though, the association between excess adipose tissue and inflammation in AS is suggested by some indirect results [25].

The connection between obesity and its effect on disease activity in AS is investigated by a few studies; therefore; we have investigated its prevalence in AS patients and its relationship with disease activity, clinical and laboratory findings.

This study showed that (63.8%) of AS patients were overweight (35.2%) and obese (28.6%), this finding is close to that of Maas et al [35] study in which 37% and 22% of cases were overweight and obese respectively and those of Durcan et al [36] in which the prevalence of overweight and obesity were 37% and 30.5% respectively.

In the present study, we have found a significant association between BMI and disease activity by using ASDAS-ESR in AS patients (p value less than 0.05).This result is close to the results that were concluded by Durcan et al. [36], Maas et al. [35], and Zepa et al [37].

According to the data of Durcan et al[36], a cohort study of forty six AS patients, (67.5%) that were overweight or obese had worse perception concerning the benefit of exercise and higher disease activity than patients normal BMI.

Those results were supported by Maas et al. study[35], a study in the population of 465 axial sponyloarthrits patients, which unveiled that obese patients had higher disease activity score than normal BMI patients [35].

In the study done by Zepa et al[37], a cross-sectional study carried on 106 patients predicted that |The higher levels of disease activity in AS patients that were overweight and

obese were notable ($p<0.05$).All these results could confirm the recommendation for AS patients to decrease BMI to appropriate level in order to achieve a high level of remission.

In comparison to other researchers who concluded that BMI is not linked with the level of disease activity and patient related outcome {Kim et al. [38] and Vergas et al. [39]}.

Data obtained from Korean study by Kim et al in a population of 789 axial SPA patients detected that increased BMI is suggestively related with the presence of syndesmophyte, but not with the disease activity in SPA patients [38]

According to data from a SPACE cohort study in 428 patients on the effect of BMI on the disease activity in axial SPA, the disease activity score is not affected by BMI in axial SPA patients [39].

These differences in these results might be explained on basis that the overweight and obesity prevalence in the last two studies were less than those of our study, 21.7% &28.5% in Kim et al. and 18.5% &11.9% in Vargas et al. study.

In the present study prevalence of peripheral arthritis, uveitis and enthesitis were (36.2%), (13.3%) and (40%) respectively. Our study revealed that the history of peripheral arthritis and extra-articular manifestation had no effect on BMI categories ($p>0.05$). This result comparable to that of Zepa et al. study [37].

In our study, we found that AS patients with increased W.C were had higher disease activity by ASDAS-ESR and these results were significant (p value less than 0.05), similar results were concluded by Aydin et al.[40], in a study of 26 AS patients, a significant correlation was established between the visceral adipose tissue using W.C and disease activity score.

There are some limitations to our study. Firstly, the relatively small sample size was conducted. Secondly, we used BMI and W.C as a measurement index for obesity and these do not precisely determine the amount of body fat.

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