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Prevalence of Metabolic Syndrome in Patients with Ankylosing Spondylitis

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Keywords: Ankylosing spondylitis; Metabolic syndrome; Prevalence

Abstract

Background: The aim of our study was to assess the prevalence of metabolic syndrome in ankylosing spondylitis (As) and identify factors that are associated with its presence.

Methods: A cross-sectional study including AS patients fulfilling the modified 1984 New York criteria for AS criteria, and age- and sex-matched controls.

MetS prevalence was assessed, using six MetS definitions (Joint Consensus, National Cholesterol Education Program 2004 and 2001, International Diabetes Federation, World Health Organization and European Group for Study of Insulin Resistance). Physical activity was assessed by the IPAQ (international physical activity questionnaire) short version. Quality of life was assessed by the SF-36 (Short Form 36).

Results: One hundred and ten AS patients were included with 68% male and median age 36 years [23-44]. The control group consisted of 100 healthy control subjects with 67% male and median age 35 years [21-44]. MetS prevalence rates varied from 8.2% to 13.6% in AS according to the definition used, when it was between 1 to 5% in the control group(p=0,01). In multivariate analysis only persists a significant association between MetS and patients ages (OR=1.12; IC [1.04-1.21]; p=0.003)

Conclusion: In this study, the frequency of MetS was observed to be higher in patients with AS than the controls for every definition of MetS. The occurrence of metabolic syndrome appears to be related to age regardless to the activity, severity and treatment of AS.

Introduction

Ankylosing Spondylitis (AS) is a chronic inflammatory disease which especially involves the axial skeletal system although it may also affect the peripheral joints and the extra-articular structures [1,2]. The definite pathogenesis of AS has not yet been determined [3].

Excess mortality has been documented in patients with Ankylosing Spondylitis (AS). The overall mortality rate in AS patients is 1.6- to 1.9-fold that in the general population, and the excess cardiovascular mortality has been estimated at 20 to 40% [4-6]. Some studies have noted an increased morbidity and mortality in AS patients compared with the general population and Epidemiological studies have produced sound evidence that the risk of cardiovascular disease is increased in patients with AS [3]. However, they cannot determine whether the risk increase is due to an independent effect of the AS or to an increase in the prevalence of conventional risk factors [6].

Metabolic syndrome main components are dyslipidemia (elevated triglycerides and apolipoprotein B (apoB) containing lipoproteins, and low High-Density Lipoproteins (HDL), elevation of arterial Blood Pressure (BP) and dysregulated glucose homeostasis, while abdominal obesity and/or Insulin Resistance (IR) have gained increasing attention as the core manifestations of the syndrome [7].

The metabolic syndrome is recognised as a cluster of cardiovascular risk factors [8]. Metabolic Syndrome (MS) is the clinical condition where risk factors for the development of cardiovascular diseases and diabetes mellitus accumulate [9]. Certain studies point to the relationship between the metabolic syndrome and the inflammation [10, 11]. It has been reported that the prevalence of MS is significantly increased in patients with inflammatory diseases like rheumatoid arthritis, psoriasis or AS than in the general population [12-17]. There is still little information regarding the prevalence of MetS in patients with AS. Few studies were conducted in European countries but no one in African countries where genetics, comorbidities and toxic habits are different. MetS has not yet been studied among patients with AS in Morocco. Therefore, the present study was designed to assess the prevalence of MetS according to all definitions currently used, in order to compare between other studies and identify the potential factors that associate with its presence.

Patients and Methods

Patients

110 consecutive patients with AS fulfilling the 1984 Modified New York Criteria who participated in the study were included [18].

Patients with other inflammatory articular diseases, malignancies, diseases of the central nervous system, chronic kidney disease, chronic liver disease besides AS, were excluded from the study.

Informed consent was obtained from all subjects and the study was approved by the ethics committee of our university.

Clinical assessments

Demographic characteristics (age, sex, weight and height and level of education), disease- specific variables (disease duration, duration of morning stiffness, the number of nocturnal awakenings, tender and swollen joint count,…) drug use (all anti-rheumatic drugs, glucocorticoid use, cardiovascular drugs and analgesics among others), comorbid conditions, and family history of rheumatic and cardiovascular diseases were documented for each patient.

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Table 1: AS characteristics.

Charactéristics	AS (N = 110)
Age (years) [1]	35.8 [23-44]
Sex(male) [2]	75 (68%)
Disease duration (years) [3]	10.3 ± 2.16
Morning stiffness (min) [3]	43.51 ± 44.60
VAS (0-100mm) [3]	44.90 ± 27.98
Axial involvement [2]	47(42.7)
BASDAI [3](0-10)	4.41 ± 2.62
BASFI [3](0-10)	5.52 ± 3.07
ESR (mm/h) [1]	20.20 [10-48]
CRP (mg/L) [1]	11.17 [7-33]
HADD [3]	9.1 ± 5.39
HADA [3]	9.59 ± 5.09

[1]: median and quartiles; [2]: number (percentage); [3]: Mean ± standard deviation; VAS: Visual Analogue (pain) Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; ESR = Erythrocyte Sedimentation Rate; CRP: C Reactive Protein; HAD: Hospital Anxiety and Depression scale

Disease activity and function

The disease activities of our patients were evaluated based on the Bath Ankylosing

Spondylitis Disease Activity Index (BASDAI) [19]. Functional status was assessed by Bath Ankylosing Spondylitis Functional Index (BASFI) [20,21]. Axial pain was assessed by VAS (visual analogue scale) and the mini-BASDAI (Question (Q)1 + Q2)+(Q5+Q6) /2]/ 3 [22].

Physical activity

The short, last-week Arabic version of the International Physical Activity Questionnaire (IPAQ) was administered, asking about the time spent being physically active in the last 7 days [23]. Minutes of sitting, walking, moderate-intensity (walking not included), and vigorous- intensity activities were counted for the last week. The items in the short IPAQ form were structured to provide separate scores on walking, moderate-intensity and vigorous-intensity activity. Computation of the total score for the short form requires summation of the duration (in minutes) and frequency (days) of walking, moderate-intensity and vigorous-intensity activities.

Quality of life

The Arabic version of the Short-Form 36 of the medical Outcome Study (SF-36), validated previously [24], was completed. The SF36 is a generic instrument providing information about eight different aspects of subjective health. The items of the SF-36 are grouped into eight subscales: physical function, limitations due to physical health problems, bodily pain, general health, vitality, social function, limitation due to emotional health problems, mental health.

Ascertainment of depression and anxiety

The Hospital Anxiety and Depression Scale (HADS) was used in patients to assess depression and anxiety. The Hospital Anxiety and Depression Scale (HADS) is a 14-item scale designed to detect anxiety and depression, independent of somatic symptoms. It consists of two 7- item subscales measuring depression and anxiety. A 4- point response scale (from 0 representing absence of symptoms, to 3 representing maximum symptomatology) is used, with possible scores for each subscale ranging from 0 to 21[25].

Body composition

Body Mass Index (BMI) was calculated from weight/ height^2 (kg/ m^2). BMI values < 18.5 kg/m^2 are considered underweight, between 18.5-24.9 as normal, 25-29.9 as overweight and values greater than 30 indicate obesity [26]. Waist Circumference (WC) was measured to the nearest 0.5 cm midway between the iliac crest and the lower rib margin. According to the International Diabetes Federation (IDF) a waist circumference value less than 80 cm indicate low risk of type 2 diabetes, coronary heart disease or hypertension [27]. The systolic and diastolic blood pressure was measured by a mercury sphygmomanometer in the sitting position after five minutes of rest.

Metabolic syndrome

The metabolic syndrome, is a cluster of classical cardiovascular risk factors (obesity, glucose intolerance, dyslipidemia, and hypertension) thought to associate with cardiovascular risk beyond the sum of its individual components [28], although this has recently been questioned.

Currently used criteria to define MetS

No consensus has been reached regarding the definition of MetS. Several groups have attempted to establish diagnostic criteria and the most widely used have been provided by the many international organizations and expert groups, such as the World Health Organization (WHO) [29], the European Group for the study of Insulin Resistance (EGIR) [30], the National Cholesterol Education Program Adult Treatment Panel III (NCEP:ATPIII) [31,32], the International Diabetes Federation (IDF) and the Joint Consensus (JC) [33,34], have attempted to incorporate all the different parameters used to define MetS.

In this study, the prevalence of the MetS was analysed according to all existing definitions (JC, NCEP 2004, NCEP 2001, WHO, IDF, EGIR) in order to establish the range of discrepancy between them. For further analysis of the predictors of the metabolic syndrome only the NCEP 2004 definition is presented, as this is most widely used definition reported in the literature, thus allowing comparisons to be drawn with other studies [32].

Biochemical measures

Venous blood samples were drawn after an overnight fast. C-reactive protein (CRP), Erythrocyte sedimentation rate (ESR), plasma glucose, total cholesterol, low-density lipoprotein (LDL) and high-density and lipoprotein (HDL) were determined by standard laboratory methods. Concentrations of total cholesterol > 5.0 mmol/L, LDL ≥ 3.0 mmol/L, HDL < 1.3 mmol/L were considered pathologic [32].

Control group

The control group consisted of 100 healthy individuals of matching age and sex groups.

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Table 2: Demographic features and laboratory findings of the AS and control groups.

Characteristics	Controls (n=100)	S (n=110)	*P value*
Age(years) [1]	34.66[21– 44]	5.8[23-44]	*0.38*
Sex male [2]	67 (67%)	75 (68%)	*0.85*
BMI (kg/m2) [3]	24.60 ± 3.28	24.17± 4.46	*0.43*
Educational level [2]			*0.0001*
-No formal education	1	17.3	
-No formal education	2	35.5	
-Secondary education	13	27.2	
- University education	84	20	
Arterial hypertension [2]	8(8)	14(12.7)	*0.26*
Diabetes [2]	4(4)	3(2.7)	*0.60*
Dyslipidemia [2]	7(7)	15(13.6)	*0.11*
Obesity [2]	5(5)	9(8.2)	*0.35*
Alcohol [2]	3(3)	11(10)	*0.04*
Smoking [2]	5(5)	26(23.6)	*0.0001*
Total physical activity [1]	2009.25[580.87-5726.25]	802.5[201.37-2152.5]	*0.0001*

[1]: Median and quartiles; [2]: Number (percentage); [3]: Mean ± standard deviation; BMI=Body Mass Index.

Table 3: Prevalence of metabolic syndrome according to definition used.

	Controls	AS N=110	*P value*
JC 2009	1%	8.20%	0.01
IDF 2005	5%	13.60%	0.03
NCEP 2004	1%	8.20%	0.01
NCEP 2001	1%	8.20%	0.01
WHO	5%	13.60%	0.03
EGIR	5%	13.60%	0.03

C: Joint Consensus; IDF: International Diabetes Federation; NCEP: National Cholesterol Education Program; WHO: World Health Organization; EGIR: European Group for the study of Insulin Resistance.

Statistical analysis

Statistical analysis was performed with SPSS 10, 0 statistical software packages. The statistical analysis of patient questionnaire data involved computation of means, medians, standard deviations, and ranges for quantitative variables; and numbers and percentages for qualitative variables. Sample t test were used to compare quantitative data and the chi-square test for qualitative data. Multivariate logistic regression models were constructed and Odds Ratios (OR) and 95% Confidence Interval (CI) were calculated to investigate the independent of the predictors of individual AS-related characteristics and MetS.

Results

Description of the AS patients

Characteristics of patients with AS are summarised in (Table 1). Patients had mean disease duration of 10.3 years ± 2.16, had mean morning stiffness of 43.51 min ± 44.60 and had mean axial pain of 44.90 mm ± 27.98 ; 42.7% of our patients had a pure axial AS. They had moderate disease activity (the mean BASDAI 4.41 ± 2.62), the mean BASFI was 5.52 ± 3.07. Regarding inflammation the median of ESR was 20.20 mm/h [10-48] and median of CRP was 11.17 mg/l [7-33].

Characteristics of the two groups

A summary of the socio-demographic and clinical characteristics of the two groups is presented in (Table 2). Both the AS and the control groups were similar in terms of age distribution (P =0.38), with median age in AS group 35.8 [23-44] and in control group 34.66 [21-44]. Most of the patients were male (68% in AS group and 67% in controls). Also there was no difference statistically significant between the two groups concerning the body mass index. Educational level was much higher in the control group compared to AS group (P=0.0001).In the AS group there were 12.7% hypertensive patients, 2.7% diabetics, 13.6% with dyslipidemia and 8.2% with obesity, whereas in control group 8% were hypertensive, 4% diabetics, 7% with dyslipidemia and 5% with obesity. There were more alcohol consumption and tobacco use in the AS group compared to controls (P<0.05). Concerning physical activity it was more reduced in AS group than controls (p=0.0001).

Prevalence of the metabolic syndrome in study population according to definition used

There was great diversity in the reported prevalence rates according to the definition used (Table 3). The prevalence of MS ranged from 8.2% to 13.6% in AS group, whereas it ranged from 1% to 5% in control group. The difference between them was statistically significant (P < 0.05).

Associations of the metabolic syndrome in patients with AS

Using the definition of metabolic syndrome according to NCEP 2004 we assessed parameters of AS that were associated with MetS in univariate and multivariate analysis (Table 4).

Table 4: Odds ratios for having the metabolic syndrome in patients with AS.

	Univariate analysis			Multivariate analysis		
	OR	*IC à 95%*	P	OR	*IC à 95%*	*P*
Age	1.13	[1.05- 1.23]	0.001	1.12	[1.04-1.21]	0.003
Disease duration	0.95	[0.77- 1.17]	0.65	-	-	-
VAS (0-100 mm)	1.02	[0.99- 1.05]	0.10	-	-	-
BASDAI	1.04	[0.80-1.34]	0.75	-	-	-
BASFI	1.03	[0.82-1.29]	0.75	-	-	-
ESR	0.97	[0.92-1.01]	0.18	-	-	-
CRP	0.96	[0.90-1.02]	0.23	-	-	-
Anti inflammatory drugs	0.84	[0.09-7.32]	0.88	-	-	-
DMARDS	1.15	[0.27-4.89]	0.84	-	-	-
Total physical activity	1.14	[0.83-1.55]	0.40	-	-	--
Mental health [1]	1.03	[1.00- 1.07]	0.04	1.01	[0.97-1.05]	0.36
HAD D	0.95	[0.84-1.09]	0.52	-	-	-
HAD A	0.92	[0.79-1.06]	0.26	-	-	-

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In Univariate analysis, it has been found association between MetS, age of patients (OR=1.13; IC [1.05-1.23]; P=0.001) and their mental health (OR= 1.03; IC [1.00- 1.07]; P= 0.04). We did not found any association with disease duration, disease activity or severity, ESR or CRP, taken disease-modifying anti-rheumatic drugs (DMARDS) or Anti inflammatory drugs (P>0.05). There was no association between MetS and total physical activity of patients and depression or anxiety (P>0.05).

In a multivariate logistic regression model it persists association between MetS and the age of patients with AS (OR= 1.12; IC [1.04-1.21]; P= 0.003).

Discussion

In this cross-sectional observational study with case control where we investigated the frequency of MetS in patients with AS, we have observed the rate of MetS in the AS patients higher than the control group, but its prevalence depends on the definition used (8.2% to 13.6% in AS group while from 1% to 5% in control group). It was found a significant relationship between MetS and the age of patients with AS but no significant relationship in term of disease duration and functional, clinical activity, inflammation or taken drugs.

The prevalence of the metabolic syndrome has varied markedly between different studies. Recently, Batmaz et al. in their study including 50 AS patients and 44 controls found a prevalence of MetS (defined with NCEP ATP III criteria) 12% in AS group against 4.5% in control groups but it was statistically no significant (P>0.05) [16]. In the study conducted by Malesci et al. including 24 patients with AS and 19 controls, the prevalence of metabolic syndrome, according to the NCEP/ATPIII criteria, was found to be considerably higher than that seen in the controls (45.8% vs. 10.5%) [15]. In another study, involving 63 patients with spondylitis receiving anti-TNF therapy and 126 controls, the prevalence of metabolic syndrome (NCEP/ATPIII criteria) was also higher among the patients than among the controls (34.9% vs. 19%) [35]. In our study the prevalence of MetS according to NCEP ATP III criteria was 8.2% in AS and 1% in control groups. These results may be comparable to the study of Malesci despite the small sample.

The factors found in this study to be independently associated with the metabolic syndrome in AS, irrespective of the definition used included older age, but there was no association with the disease duration, disease activity or inflammation measured by ESR and C reactive protein. The association with older age is not surprising, because in the general population the MetS has been shown to affect primarily older subjects, as a consequence of age-related modification of some of its components [36]. Allowing comparison of our results with those of other studies in AS and other conditions, in the literature, Papadakis et al. have also observed that the AS patients with MetS are older than the AS patients without MetS; their disease duration was longer and they had higher BASDAI scores and cardiovascular risks [14]. In the study of Batmaz et al. they did not observe any statistically significant relationship between the presence of MetS and the disease duration, the BASDAI and the BASFI values [16]. In Malesci study the investigators have not detected any statistically significant relationship between the presence of MS in the AS patients and their ages, disease duration and BASDAI and BASFI results [15].

This study has several strengths. These include the use of all of the existing MetS criteria for the first time in Morocco patients with AS, it includes case-control. Despite this the most prominent limitation of our study was the cross-sectional design and selection bias cause Tertiary center that recruits the most severe forms of AS and this do not reflect the reality of AS rheumatism in Morocco. Further and wider ranging clinical studies are thus needed in order to evaluate the presence of MetS in patients with AS.

Conclusion

In summary this study shows that the ankylosing spondylitis has been associated with increased prevalence of MetS. Older age was independent predictor associated with the presence of MetS in patients with AS. These findings suggest that clinicians should screen for MetS in patients with early AS to control its components and, therefore, reduce their risk of cardiovascular diseases.

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