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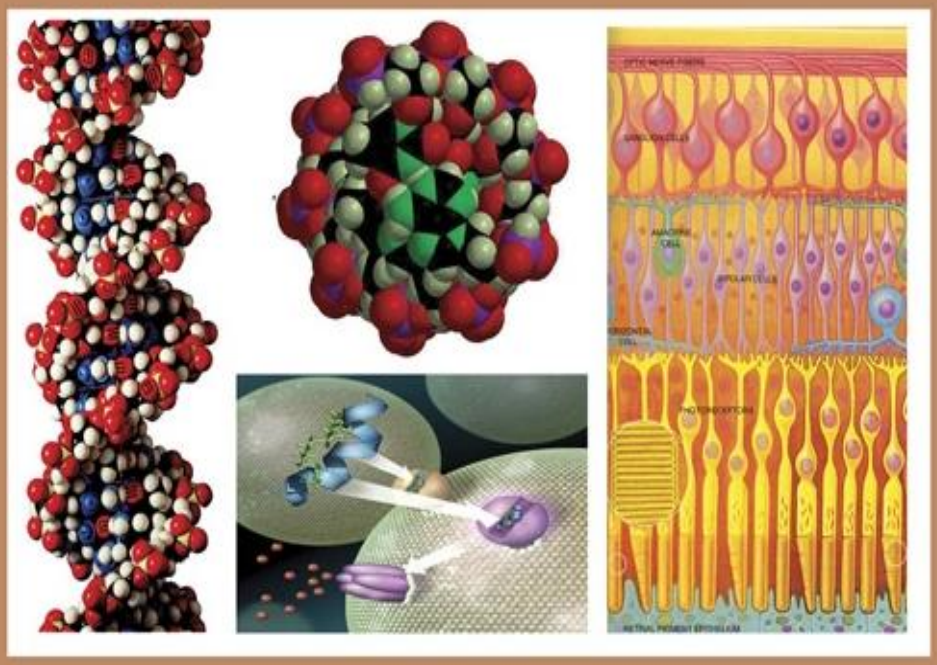

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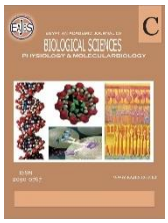

Late Onset Ankylosing Spondylitis: Clinical and Biological Features Comparison With Early-Onset Patients

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ABSTRACT

Background: Ankylosing spondylitis (AS) is an inflammatory disease that affects the spine and sacroiliac joints and is connected with the human leukocyte antigen (HLA)-B27. Late-onset AS is characterized by severedisease-marked elevation of laboratory measurements of inflammation, and more frequent involvement of the peripheral joints and the cervical spine as compared with early-onset AS**Objective**:This topic aimed to study the clinical, radiological, and biological profile of Algerian patients presenting Late-Onset Ankylosing Spondylitis in comparison with patientswith Early-Onset Ankylosing Spondylitis.**Methods:** 292 patients diagnosed with AS at the level of rehabilitation department of Hassani AEK hospital of Sidi bel abbes region were enrolled. Studied parameters were: age, disease duration, morning stiffness, joint involvements, laboratory data, disease activity, and treatments. All data were processed and analyzed via SPSS 20.0 (Statistical Package for the Social Sciences, IBM Corporation, Chicago, IL August 2011). **Results**: A total of 247 patients had early-onset AS, while 45 had late-onset AS. The Age Onset Ankylosing Spondylitis was associated significantly with age and disease duration $p<0.0001$, the average mean duration morning stiffnesswas higher in a group of late-onset age 8.00±0.000 years VS 6.91±4.288 years. However, acute inflammation was more noted in theLoAS group (93.3% Accelerated ESR and 60% positive CRP) and 93.3% of positive HLAB27 was noted in this late group with p=0. 049. Whereas, the group of early-onset age suffered more from their cervical 40.4% and lumbar 74.4% and, theywere the most affected in their peripheral joints (knees affection 14.1% vs 0% and hips affection 32.9% vs 6.7 %, p=0.033). Furthermore, high disease activity indices were more noted in this young group (BASDAI 2.984±1.942 VS 2.194±0.774 and ASDASCRP 2.659±1.309VS 2.106±1.091). Uveitis (AAU) was the most common comorbidity reported in both groups and the Sulfasalazine and Humira treatment was the most received in each group but the methotrexate treatment was more used by the early-onset AS p=0.038.**Conclusion:** In our study, the late-onset group exhibits higher levels of inflammation and more positive HLAB27 than the early group, which was more affected by extra-articular damage, lumbar pain, and peripheral joints. The late and early age onset groups had different AS characteristics.

INTRODUCTION

Ankylosing spondylitis (AS) is a persistent inflammatory disease that mostly affects the spine and sacroiliac joints and is connected with the human leukocyte antigen (HLA)-B27; its frequency varies from 0 to 1.9% (Jung YO *et al.*,2010). The sacroiliac joints are typically affecte d, as is the spinal column to a different a mount,
and to a lesser extent, the peripheral joint s (RugienneR et al.,2008).Themedical evidence for AS is well recognized, but there is little data on how the disease generally affects the subjective health of those who are affected (Dagfinrud H.*et al.*,2004). The major joints are thought to be the most frequently involved, with the hips, shoulders, knees, wrists, and metacarpophalangeal (MCP), metatarsophalangeal (MTP), and proximal interphalangeal (PIP) joints recorded in decreasing order of occurrence (Cohen M.D. *et al* .,1982).The clinical expression of some inflammatory diseases, including the presenting manifestations, clinical evolution, and prognosis, may depend on the age at onset.Clinical onset of AS after the age of 50 years is uncommon. Late-onset AS is characterized by severe disease-marked elevation of laboratory measurements of inflammation, and more frequent involvement of the peripheral joints (predominantly the shoulders) and the cervical spine as compared with early-onset AS (MontillaC.*et al* .,2012; Caplanne D.*et al* .,1997; Calin A.*et al.*,1991).

The objective of our study was to examine late and early age onset differences of manifestations associated with ankylosing spondylitis in Algerian patients

MATERIALS AND METHODS

Population:

Our survey covered 292 patients diagnosed with late (LoAS) and early(AoAS) onset ankylosing spondylitis at the Functional Rehabilitation department of Hassani Abdelkader University Hospital of Sidi Bel Abbes region between 2018 and 2021.

Methods:

We looked at a variety of factors, including, age, disease duration, morning stiffness, medical history, articular and extra-articular injuries, laboratory data, and favorable outcomes, AS patients' HLAB27, disease activity markers, and treatment.

Statistical Analysis:

We were able to calculate theMean and standard deviation (Mean±SD)using Simple T-test. The significance of frequency (percentage) differences was determined by the Chi-square test.All statistical analyses were performed using IBM SPSS statistics version 20.The level of significance was set at 5%.

RESULTS

In our survey, 247 patients were diagnosed with early-age onset AS (AoAS) and 45 patients with late-age onset AS (LoAS). The mean age of patients was 36.89±10.839 years vs 63.67±2.526 years with a significant relationship $p<0.0001$. Same case with anaverage mean of disease duration which was highly significant in the late age onset AS $p<0.0001$. Accelerated ESR and positive CRP were high in the late age onset comparedwith the other group (93.3% VS 82.3%, 60% VS 57% respectively) with no association $p=0.270$ $p= 0.821$. Prevalence of HLA-B27 antigen was highly associated with late age onset $p=0.049$. Moreover, we found that the earlygroup contains the highest prevalence of smokers 10.1% VS 0% and they suffered more from their spine, peripheral joints and very high disease activity.

Besides, both patients group (LoAS and AoAS) were affected by uveitis at 34.3% and 33.3% respectively. However, we did not record any prevalence of psoriasis-crohn’s disease-diabetes-renal failure in the late-onset group. Humira was the most treatment used in each group (229(82.7%) VS 12(80%)) (Table 1).

Table 1: demographic, laboratory data, radiologic and treatment of Ankylosing spondylitis patients based on Age-at-onset.

Characteristics (Mean±SD) or n(%)	Early-onset (AoAS) ≤ 50 Years	Late-onset LoAS ≥ 51 Years	P value
Age	36.89±10.839	63.67±2.526	**<0.0001**
Disease duration	6.91±4.288	8.00±0.000	**<0.0001**
Duration morning stiffness	25.16±26.765	24.00±27.659	0.819
Laboratory data			
ESR titer (mm/h)	45.561±28.800	46.633±28.719	0.485
Accelerated ESR	228(82.3%)	14(93.3%)	0.270
CRP titer (mg/l)	19.864±23.325	16.773±17.453	0.250
Positive CRP	158(57%)	9(60%)	0.821
HLAB27	193(69.7%)	14(93.3%)	**0.049**
Smoking	28(10.1%)	00(0%)	0.195
Spine damage			
Cervical	112(40.4%)	5(33.3%)	0.585
Lumbar	206(74.4%)	10(66.7%)	0.508
Radiologic joint damage			
Knees	39(14.1%)	00(0%)	0.118
Hips	91(32.9%)	1(6.7%)	**0.033**
Disease activity indices			
BASDAI	2.984±1.942	2.194±0.774	0.099
ASDASCRP	2.659±1.309	2.106±1.091	0.613
Disease activity			
Inactive	60(21.7%)	5(33.3%)	
Moderate	59(21.3%)	3(20%)	0.484
High	129(46.6%)	7(46.7%)	
Very high	29(10.5%)	00(0%)	
Extra-articular damage			
Uveitis	95(34.3%)	5(33.3%)	0.939
Psoriasis	10(3.6%)	00(0%)	0.454
Crohn's disease	5(1.8%)	00(0%)	0.600
Diabetes	5(1.8%)	00(0%)	0.600
Renal failure	3(1.1%)	00(0%)	0.685
Medical treatment			
Methotrexate	17(6.1%)	3(20%)	**0.038**
Sulfasalazine	224(80.9%)	11(73.3%)	0.473
NSAIDs	34(12.3%)	1(6.7%)	0.515
Biological treatment			
Humira	229(82.7%)	12(80%)	0.791
Remicade	21(7.6%)	3(20%)	0.088
Enbrel	21(7.6%)	00(0%)	0.268

DISCUSSION

Our investigation looked to study two groups of Algerian patients based on age onset AS; certain differences between LoAS and AoAS were noted.

We analyzed the relationship between various AS parameters in Late Age Onset Ankylosing Spondylitis (LoAS) and Early Age Onset Ankylosing Spondylitis (AoAS) in Algerian patients. We found that the late one was characterized by a high average mean of disease duration of 8.00±0.000 vs 6.91±4.288 in discordance with the results of (Montilla C.*et al.*,2012) showing the higher duration of the disease in the early-onset group in relation to AS progression. A positive association was reported between the two groups ($p<0.0001$) identically to (Chen *et al.*,2012) findings $p<0.0001$.

As the studies of (Montilla C.*et al.*,2012; Chen H.A.*et al.*,2012) we did not show a significant association between erythrocyte sedimentation rate (ESR) titer (mm/h) and age onset $p=0.051$, $p=0.618$, $p=0.485$ respectively. The same case for C-reactive protein (CRP) titer (Chen H.A.*et al.*,2012). (Montilla C.*et al.*,2012) found that

patients with late-onset disease had more cervical and dorsal pain, anterior chest wall involvement, and raised ESR.Besides,the early-onset group was found to have a high CRP titer which signifies a high degree of inflammation expressed by severe axial involvement and a very severe disease state as assessed by BASDAI and ASDASCRP activity indices. Similarly, (Benhamou M.*et al.*,2010) data noted a high frequency of increased CRP in patients with painful axial AS and confirmed the validity of CRP as an outcome measure reflecting the degree of inflammation in AS.

On the other hand, we found a high prevalence of positive HLAB27 (human leucocyte antigen) in a group of Late-onset 93.3% with significant relation p=0.049 contrary to (Caplanne D.*et al.*,1997) findings.

Concerning the spine injury, the lumbar joint was affected in the majority of early-onset AS group 74.4% and whether the age onset was early or late, any positive difference was seen in axial symptoms (cervical p=0.585, lumbar p=0.508) in discordance with (Caplanne D.*et al.*,1997) findings p= 0.002. (Montilla C.*et al.*, 2012) found that the involvement of the cervical spine was frequent in the older group both at the onset of the disease with significant association p=0.005. The patients who suffered from early age onset were more affected in their hips 32.9%. Furthermore, we found an association between peripheral affection and age of onset p=0.033, as demonstrated by (Chen H.A.*et al.*, 2012) findings of p=0.004. (Montilla C.*et al.*, 2012) provides further evidence for the existence ofdifferent clinical patterns between late-onset and early-onsetsubsets of patients with AS, and evidence that mixed forms(axial and peripheral) are more frequent in the clinicalexpression of AS after 50 years of age. The Early-onset group was characterized by a higher occurrence of peripheral arthritis. (Brophy S.*et al.*, 2002) show that progression of radiographic findings is a functionof disease duration.

Our findings back up the link between age onset and disease activity indices, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDASCRP) scores were considerably higher in the early-onset AS group 2.984±1.942, 2.659±1.309 respectively. We did not reveal an association between BASDAI and age onset p=0.099 similar to (Chen HAet al.,2012)with results of p=0.708. There are some researchers demonstrated that early-onset AS patients had higher average BASDAI with negative association (Montilla C.*et al.*,2012); it did not appear to have a significant role in the development of AS. Regardingthe extra-articular manifestations, acute anterior uveitis (AAU) was noted in both groups at 34.3% vs 33.3%; according to (Calin A.*et al.*,1991; Caplanne D.*et al.*,1997; Chen H.A.*et al.*,2012) results, uveitis was not significantly related with age onset p=NS, p=NS, p=0,819 respectively, which agree with our findings p=0.939. Similarly, for psoriasis, any correlation was found tobe p=0.454 as to some literature findings (Caplanne D *et al.*,1997). We found in our study that the early-onset AS group used more drugs than the late-onset AS group. Moreover, we demonstrate a significant treatment effect of the methotrexate on the age onset p=0.038; the reason behind this through the study is that this disease activity is more than the others.

Our study adds to the growing body of data that the late-onset and early-onset subsets of AS patients exhibit distinct clinical patterns.It appears that other investigations are required to validate these findings and pinpoint particular AS disease characteristics concerning the age onset.

Conclusion:

In our research, the late-onset group expresses a high level of inflammation and more positive HLAB27 than the early ones who have lumbar pain, knees, hips, and extra-articular injury more affected. It's imperative to carry out additional research.

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Conflict of interest declaration: The authors have declared that there are no conflicts of interest.

Ethics Approval: The Medical Committee of Sidi bel Abbes University Hospital and the Biology Department of DjillaliLiabes University approved the study.

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