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Clinical and Epidemiological Aspects of Ankylosing Spondylitis Patients in a Single Center in Baghdad

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Abstract

Ankylosing spondylitis is a chronic inflammatory disease with axial involvement but also may present as a peripheral arthritis and extraarticular manifestations.
Objective: To assess clinical aspects of ankylosing spondylitis patients and different associated demographic variables in Baghdad teaching hospital.
Patients and methods: A cross-sectional study was carried out in Baghdad teaching hospital which includes 402 patients (≥ 18 years old) with a clinical diagnosis of AS according to Assessment of Spondylo Arthritis International Society for AS were involved in this study from June/2019 to June/2021. Demographic data and disease characteristics, presence of extra-articular manifestations (past and present) and measurement of disease activity was done by BASDAI, erythrocyte sedimentation rate (mm/h) and C-reactive protein (mg/L). In addition, HLAB27 typing was reported. Results: The age of onset for males was 24.87±8.8 and for females25.97±8.6 years, HLA typing HLA-B27 were 49.55% and 35.38% in males and females respectively and the association was found to be statistically significant (P. value =0.031). While family history was reported at 25.82% and 34.33% in males and females correspondingly. 75.07% of males compared to 71.38% of females were treated with Anti TNF therapy. Females had later onset of disease than males with lower percentage of HLA B27 positivity. Recommendation: more comprehensive assessment with advanced diagnostic and treatment standards.

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Keywords: Ankylosing Spondylitis; Gender; HLA B27 Positivity; Uveitis; Disease Activity.

1. Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disorder, described by low back with buttock pain and associated with morning stiffness of insidiously onset, frequently begins in the youth or early adulthood [1]. AS a pattern of spondyloarthritis, is a common chronic inflammatory disorder upsetting both of sacroiliac joints and spine with or without peripheral arthritis and other systemic manifestations that have burden on the quality of life and health status. The cause of AS is still unclear, and genetic risk factors, including HLA-B27, has been suggested to implicate with AS pathogenesis [2]. Correspondingly, endoplasmic reticulum aminopeptidase 1 (ERAP1) is another genetic factor that has been revealed to have an important role in the pathogenesis of AS and take part in presentation of peptide trimming by the major histocompatibility complex. Environment is another causative factor involving infection and stress [3]. Sacroiliitis with syndesmophyte formation can in advanced disease lead to spinal ankylosis or spinal fusion with formation of so-called bamboo spine [4] with subsequent limitation of movement and functional impairment. Ethnic, terrestrial, and socio-economic aspects have been related with the clinical pattern of the disease [5].
The clinical features and patterns of the disease seem to differ from one country to another. In demand to review the patterns of AS, many articles have been done worldwide throughout the past many decades. One of the best of studies were built on cohorts from America [6]. At present, the most common investigations for AS patients are acute phase reactants measurements such as erythrocyte sedimentation rate (ESR) and also C-reactive protein (CRP), and imaging by plain radiographs and/or Magnetic resonance imaging (MRI) of the sacroiliac joints, in addition to genetic testing for HLA-B27.Though, each of these tests has limitations.

Nomenclature & Symbols			
AS	Ankylosing Spondylitis	ERAP1	Endoplasmic Reticulum Aminopeptidase 1
ESR	Erythrocyte Sedimentation Rate	CRP	C-Reactive Protein
MRI	Magnetic Resonance Imaging	ASAS	Assessment of Spondylo Arthritis International Society
AU	Anterior Uveitis	IBD	Inflammatory Bowel Disease
SPSS-15	Statistical Packages for Social Sciences- version 15		

The presence of gender-attributable variances in AS patients concerning disease features, radiological damage, clinical conclusion and reaction to treatment has been advocated [7]; furthermore, a steady drop in the ratio of male–female has been described in the AS patients. Generally, the females presented with less structural destruction and low prevalence of radiographic progression of spine and sacroiliac joints. Moreover; a radiographic changes of sacroiliac joints take a longer time than males to develop and frequently associated with a delayed diagnosis [8].

1.1. Aim of the study

To assess clinical aspect of ankylosing spondylitis patients and different associated demographic variables in Baghdad teaching hospital.

2. Patients and Methods

A cross sectional study was carried out in Baghdad teaching hospital/ rheumatology unit enrolling 402 patients with (≥ 18 years old) and a clinical diagnosis of AS according to ASAS (Assessment of Spondylo Arthritis International Society) [9] were involved in this study from June/2019 to June/2021. Demographic data and disease characteristics, enthesitis, dactylitis and presence (past and present) of extra-articular manifestations [psoriasis, anterior uveitis (AU), inflammatory bowel disease (IBD)]. Furthermore, family history of first or second degree relative with AS, psoriasis, AU, IBD or reactive arthritis was reported. Measurement of disease activity was by BASDAI and erythrocyte sedimentation rate (ESR) (mm/h) C-reactive protein (CRP) (mg/L) and also HLAB27 were reported. The BASDAI comprises of 6 domains involving fatigability, back pain, pain/swelling of peripheral joint, enthesitis, and duration of morning stiffness.
The present and previous use of medications such as (non-steroidal anti-inflammatory drugs, analgesic, biological and synthetic disease-modifying anti-rheumatic drugs) was documented.
Informed consent was obtained from patients in accordance with the declaration of Helsinki with the approval of all participants in the study and data were accessible from unit registry and routine patient cares with no further procedures done for this study.

3. Statistical Analysis

Analysis of data was carried out by using the available statistical package of SPSS-15 (Statistical Packages for Social Sciences- version 15). Data were existing in simple measures of mean, standard deviation, and range (minimum-maximum values) using independent student-t-test for difference between two means, while different percentages (qualitative data from different groups and from control group) were tested using chi-square test (2-test). Statistical significance was considered whenever the P value was equal or less than 0.05.

4. Results

A total of 402 of Ankylosing spondylitis patients attending Baghdad teaching hospital rheumatology unit during the period of study were enrolled in the study with mean age of study sample were (39.08±9.4) years for males and (37±8.8) years for females with distinct males' preponderance. The age of onset for males was (24.87±8.8) and for females (25.97±8.6). HLA-B27 positivity were (49.55%) and (35.38%) in males and females correspondingly and the association was found to be statistically significant (P. value =0.031). Only (45%) of patients have HLA typing (181 out of 402). While family history was reported in (25.82%) and (34.33%) in males and females respectively. (75.07%) of males compared to (71.38%) of females treated with Anti TNF therapy. Higher percentages of patients (71.51 %) & (72.32%) for males and females correspondingly had morning stiffness. Co-morbidity was reported in (21% & 20%) for males and females respectively. Females shows higher frequency of ESR positivity (68.3 %) compared to (55.4%) for males and the association was found to be statistically significant (P. value =0.031) as shown in table 1.

Table 1 The distribution of study sample by demographic and clinical aspect and gender

Demographic &clinical aspect	Gender		P-value
	Males (n =337)	Females (n =65)	
Age, mean SD (years)	39.08±9.4	37±8.8	0.121
Age of onset, mean SD, years	24.87±8.8	25.97±8.6	0.695
Duration median, years	6	8	0.125
Age of diagnosis, mean SD, years	30±9.6	33±9.5	0.232
HLA typing HLA-B27 positivity%**	49.55	35.38	0.332
Active peripheral arthritis%	8.24	16.2	0.021*
Family history %	25.82	34.33	0.113
Anti TNF %	75.07	71.38	0.959
Morning stiffness %	71.51	72.32	0.896
Co morbidity %	21	20	0.356
CRP +	39.1	40.2	0.123

ESR+	55.4	68.3	0.031*
BASDAI ≥4 %	17.1	14.2	0.221

*significant P value ≤ 0.05

**Only 181/402 of patients have HLA typing (45%)

HLA typing and clinical aspect: HLA positive patients had younger age of onset (25.18±8.53) compared (32.89±8.71) in negative patients with significant difference (p-vale =0.027). Also had higher frequency of ESR and CRP positivity. Moreover; the patients with positive HLA B 27 showed more active disease measured by BASDAI ≥4 (18.2% vs 14.2%) and a higher frequency of uveitis (20.58% vs 14.38%). The HLA B27 negative revealed a higher frequency of active peripheral arthritis (19% vs 12%). While non-significant differences were observed between positive & negative HLA typing regarding age, duration, age at diagnosis and co-morbidity as shown in table 2.

Table 2 The distribution of study sample by demographic &clinical aspect and HLA B 27Typing

Demographic &clinical aspect	HLA B 27 Typing (n=181)		P-value
	Positive (n=114)	Negative (n =67)	
Age, mean SD, years	37.34±9.03	39.34±10.12	0.154
Age of onset, mean SD, years	25.18±8.53	32.89±8.71	0.027*
Duration median, years	8	6	0.147
Age of diagnosis, mean SD, years	33±8	35±9	0.331
Active peripheral arthritis %	12	19	0.012*
Anti TNF %	15	17	0.125
Morning stiffness %	88.33	77.53	0.876
Comorbidity	23	16	0.687
CRP +	45.4	32.6	0.653
ESR+	61.2	57.2	0.524
BASDAI≥4 %	18.2	14.5	0.014*
Anterior uveitis %	20.58	14.38	0.041*

*significant P value ≤ 0.05

Onset of disease (early versus late onset): significant differences in age, age of onset, duration, age at diagnosis, level of positivity of CRP, ESR while non-significant differences was found regarding Anti TNF, and morning stiffness and co-morbidity. The patients with early onset AS diagnosed early in their life with more duration of the disease with a higher frequency with of duration of morning stiffness (88.33% vs 77.53%) and a higher positivity of ESR and CRP (88.4% and 50.6% vs 51.2 and 42.6%). The late onset AS revealed a higher frequency of peripheral arthritis (13% vs 8%) and less use of Anti TNF (14% vs 17%) and more comorbidities (24% vs 8%) as seen in table 3.

Table 3 The distribution of study sample by demographic & early and late onset

Demographic and clinical aspects	AS		P-value
	Early onset	Late onset	
Age, mean SD, years	20.31±9.03	31.34±8.12	0.001*
Age of onset, mean SD (years)	15.18±8.53	29.89±8.71	0.003*
Duration median, years	8	4	0.04*
Age at diagnosis, mean SD, years	19±8	32±9	0.002
Active peripheral arthritis %	8	13	0.003*
Anti TNF %	17	14	0.125
Morning stiffness %	88.33	77.53	0.876
Co morbidity	8	24	0.05
CRP +	50.6	42.6	0.653
ESR+	88.4	51.2	0.023*
BASDAI≥4 %	18.2	12.5	0.014*

5. Discussion

The mean age of onset (24.87±8.8) for males and (25.97±8.6) for females which had later onset of disease than males. These results are similar to other described studies by Landi et al 2016 [10] and Jong et al., 2020 [11] who demonstrated that men had a marginally earlier onset of the disease than women. It was also different from Lee et al., 2007 who reported that female patients with earlier onset [12]. AS has been observed as a disease upsetting men as thought previously but new studies revealed a decrease ratio of male: female from 10:1 to about 2-3:1 [10]. An

analysis of 13 cross-sectional articles showed the gender ratio of 3.4:1 with some variations between different geographical areas [13]. Although the results of this study showed a male predominance but less than Landi et al 2016 [10]. The current study showed that males represent (83.83%) while female (16.17%) of study sample. However, as the progress of diagnostic radiographic apparatus [14, 15] improve the diagnosis and also change the diagnostic criteria with addition of MRI to these criterions. Initial and right diagnosis and subsequent aggressive therapy with AS are essential to decrease the probable destructive effects of the disease [16] and slow progression of structural damage with less impact on health status with subsequent better quality of life.

Regarding HLA typing higher percentage was found in males (49.55%) compared to (35.38%) in females and the association were found to be statistically significant. This result is in agreement with what had been recorded in China by Yang et. al. 2013 [17] and differ from other reported studies [18, 19]. And this may be due to geographical differences. Although this study demonstrated that female patients with AS have a higher percentage of peripheral arthritis than male patients but it was statistically non-significant (16.2% vs 8.2%) and these findings are consistent with de Jong et.al., 2020 [20] who found a slightly higher percentage of peripheral arthritis among female patients compared to males.

ESR and CRP are inflammatory mediators which are commonly used in the evaluation of inflammatory diseases, including AS, through daily clinical assessment [21]. This current study revealed that females with higher percentages of CRP and ESR positivity, demonstrating more severe inflammation, which agrees with the results of de Jong et.al., 2020 [19] and different from other studies [22, 23]. Both ESR and CRP are acute phase reactant but they are affected by factors other than parameters of disease activity. Although CRP are less affected and more sensitive, moreover; ESR are increased with aging and is higher in women than in men [24]. Other confounding factors are drugs such as non-steroidal anti-inflammatory drugs that affect markers of inflammation.

The BASDAI in the present study revealed that higher percentages in males related to females. This result is similar to what had been recorded by Swinnen et al. [2018], who found that BASDAI were worse in males, even if they accepted that increment of probability of prevalent axial and peripheral joint pain among women [25] and differ from de Jong et.al., 2020 [20] who demonstrated a higher BASDAI among female patients than males. In another study, there was no difference regarding disease activity or physical function over time between gender and differ from other reported study by Webers et.al. 2016 [23]. Remarkably, this study reported a higher BASDAI among males but also reported a diverging results where female patients with a higher ESR and CRP in reverse to Webers et.al. 2016 [23] who found male patients with a higher levels of CRP but with lesser BASDAI. Still the studies demonstrated a conflicting results regarding differences among both genders in patients with AS.

Several studies suggested a solid relationship between AS and HLA B27 and many features of the disease particularly gender, family history, age of onset and some clinical findings affected by HLA B27 [26]. The present study demonstrated that patients with HLA B27 had higher percentages of anterior uveitis, earlier onset and more active disease measured by BASDAI with more axial involvement compared to HLA-B27 negative patients with significant differences this result is similar to other reported studies [15, 17, 27, 28]. Whereas peripheral arthritis reported more with negative HLA B27 consistent with [20].

The current study revealed that patients with early onset of the disease had a higher percentages of morning stiffness, positivity both of ESR and CRP, BASDAI with more axial involvement and less peripheral arthritis consistent with the findings of Montilla et. al., 2012 [29]. Involvement of axial spine may help in early diagnosis and avoid diagnostic delay with early treatment and better outcomes and quality of life. The importance of early diagnosis nowadays becomes a challenging matter because the effective treatment is offered and early use of anti-TNF drugs is more effective with better consequences. The non-radiographic axial spondyloarthritis is not discussed in this study.

6. Conclusion

Females had later onset of disease than males (25.97±8.6 vs 24.87±8.8) respectively while males had higher percentage of HLA typing 49.55% compared to 35.38% in females. The BASDAI in this study higher percentage in males compared to females. Higher percentage in HLA positive with anterior uveitis in comparison to HLA-B27 negative patients, there were no differences in disease activity and physical function with time between both genders.

7. Recommendation

The researchers need to develop more comprehensive and systematic research with advanced diagnostic and treatment standards. Advances in detections on the etiopathogenesis of the disease will improve comprehensive management of the disease.

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