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THE RELATION OF HLA-B27 TYPING WITH OTHER BIOMARKERSIN IRAQI PATIENTS WITH ANKYLOSING SPONDYLITIS

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ABSTRACT

Sixty (60) patients were included in this study, were diagnosed as established AS patients who were attending the rheumatology outpatient clinic of Baghdad teaching hospital, thirty (30) patients of them were on conventional treatment (steroid and/or cytotoxic drugs), while the other thirty (30) patients were on biological treatment (infliximab infusion).The Human Leucocyte Antigen B-27 waspositive in 34 (56.7 %) patients, and in no subject (0%) from controlgroup and this difference is highly statistically significant (P- Value <0.0001) and there is a significant difference of high sensitivity C-ReactiveProtein between positive and negative Human Leucocyte Antigen B-27groups (P-value =0.0437) and no other differences detected of(matrix metalloproteinase-3, Bath Ankylosing Spondylitis Disease Activity Index, Bath AnkylosingSpondylitis Functional Index) between positive and negative HumanLeucocyte Antigen B-27 patients groups.The study shown thatthesensitivity and specificity of theHuman Leucocyte Antigen B-27 test was 56.6 % and 100 % respectively and there is a significant statistical difference of high sensitivity C-Reactive Protein between positive and negative Human Leucocyte Antigen B-27 patients groups.

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INTRODUCTION

Ankylosing spondylitis (AS) is the prototypic form of spondyloarthritis, a family of disorders characterized by inflammation around the entheses (the sites of ligament insertion into bone), an association with the human leukocyte antigen (HLA)-B27, and radiographic sacroiliitis (Reveille, 2012). The most characteristic feature of AS is new bone formation leadingto ankylosis of the sacroiliac joints and syndesmophytes in the spine. Since thesymptoms of inflammation and the acute phase response responddramatically to treatment by tumor necrosis factor (TNF)-alpha blockers, it was expected that theradiographic progression in these patients would also be arrested by TNFblockade, as it is in rheumatoid arthritis (van der Heijde, 2009). HLA-B27 is an HLA-B allele of the major histocompatibility complex class I molecules. Even before the quaternary structure of HLA-B27 and other HLA class I alleles had been resolved, it was known that a major function of HLA class I molecules is to present antigenic peptides to the T cell receptors of CD8+ T lymphocytes (Chou, 2006). In general, there is a clear correlation between the prevalence of AS in a given population and the prevalence of human leukocyte antigen (HLA)-B27 in that group, with the prevalence of AS being approximately 5 to 6 percent among people who are HLA-B27-positive (Dean, 2014). Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) questionnaires are widely used to evaluate disease activity and physical function, respectively, in patients with AS, and both are often applied in medical and clinical researches (Song, 2008). C-Reactive Protein (CRP) is a blood protein that measures inflammation or infection. This marker reflects systemic inflammation in chronic disorders including Rheumatoid Arthritis, Psoriatic Arthritis, Crohn's Disease, Ulcerative Colitis, Ankylosing Spondylitis and other chronic health conditions (Kruithof, 2005).

MATERIALS AND METHODS

Kits and reagents: *HLA B27 Real-TM kit (Sacace BIOTECHNLOGIES, Italy), ReliaPrep Blood gDNA Miniprep System (Promega, USA).High* Sensitivity C- Reactive Protein Nephelometry kit(*Genrui Biotech Inc., China),Human matrix metalloproteinase-3 ELISA kit (SHANGHAI YEHUA, China),*

Patients: Sixty patients (55 males and 5 females) were attended to medical city, Baghdad teaching hospital, Department of Rheumatology outpatient clinic and biological therapy unit included in this study during period from beginning of October 2016 till end of October 2017, their mean age ± Standard deviation (SD) was (40.05 ± 8.02 years), thirty (30) patients of them treated with biological agent (intravenous infusion of Infliximab of 5mg/kg), and other thirty (30) patients treated with conventional treatment (steroid and/or cytotoxic drugs).

MATERIALS AND METHODS

From each individualthree (3) ml of venous blood was aspirated,two milliliters (1ml) of sample was put in ethyelenediaminetetraacitic(EDTA) tubes for HLA B-27 testing and other (2) ml let clot at room temperature, then centrifuged to separate the serum which was collected in aliquots to store in(- 20 ºC) until needed for investigation of hs- CRP and MMP-3.

Statistical Analysis: Statistical analysis in this study was done using SPSS version computer software 20. T test was used to analyze the data, and calculation of mean difference, Fisher exact and Chi-square test for comparison of proportion, P-value of less than 0.05 was considered as statistically significant, P-value < 0.01 as highly significant and P-value < 0.001 as extremely significant.

RESULTS

This study was included sixty (60) patients with AS, fifty five 55 (91.6%) males & five 5 (8.4%) females, the male to female ratio was 11:1 as shown in Figure-1.

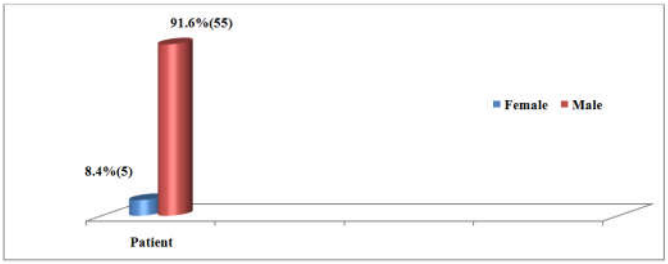

Figure 1. Distribution of patients according to their gender

The study included (60) patients, their mean age ± Standard deviation (SD) (40.05 ± 8.02 years) and (30) apparently healthy subjects, their mean age ± SD (40.07 ± 7.20 years) as shown in Table-1.

Table 1. Distribution of mean age with ± standard deviation for patient and control groups

Group	Number	Mean (year)	Standard deviation
Patients	60	40.05	± 8.02
Controls	30	40.07	±7.20
P- Value=0.99			
Not statistically significant			

HLA-B27 positive in 34 (56.7 %) patients, and in no subject from control group and this difference is highly statistically significant (P- Value < 0.0001) as shown in Figure-2. There is a significant statistical difference of hs-CRP between positive and negative HLA B-27 groups (P-value=0.0437) and no other differences were detected of (MMP-3, BASDAI, BASFI) between positive and negative HLA B-27 patients group as shown in Table-2

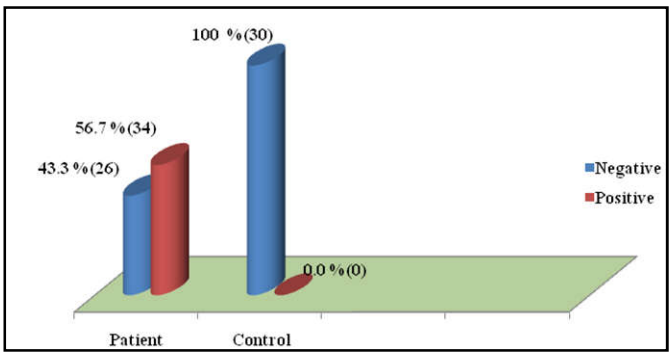

Figure 2. HLA B-27 distribution in patient and control groups

Table 2. Correlation between HLA-B27 positive and negative groups With hs-CRP, MMP-3, BASDAI and BASFI in patients groups

	HLAB27	Number	Mean	Standard Deviation
MMP-3	Positive	34	4.4729	3.3705
P=0.8964	Negative	26	4.3681	2.6420
hs-CRP	Positive	34	10.8726	10.2076
P=0.0437	Negative	26	16.5677	11.1049
BASDAI	Positive	34	3.626	2.120
P=0.8205	Negative	26	3.512	1.660
BASFI	Positive	34	4.132	2.185
P=0.9530	Negative	26	4.104	1.282

Table 3. Serum levels of hs- CRP (mg/L) in patients group according to type of treatment

Group	Conventional Treatment	Biological treatment (Infliximab)
Number	30	30
Mean (mg/L)	16.16	10.51
Standard deviation	± 12.40	±8.41

P-value= 0.0438
Statistically significant

Mean serum level of hs- CRP (mg/L) higher in patients treated with conventional treatment, than in patients on biological treatment (infliximab infusion) and this difference is statistically significant (P-value = 0.0235) as shown in Table-3.

DISCUSSION

Ankylosing spondylitis (AS) is a potentially disabling chronic inflammatory condition affecting the axial skeleton that is manifested by chronic back pain. The onset is typically before 45 years of age (BASDAI, 2008). This study included sixty (60) patients with ASwho attended the rheumatology consultation clinic of Baghdad teaching hospital in the period between October 2016 to October 2017, thirty (30) of them treated with biological treatment and other thirty (30) treated with conventional treatment. Regarding the gender variation in the susceptibility to AS patients reported by the present study which showed that the disease is more predominant in males than in females with a ratio of 11:1, this result nearly in agreement with local study done by Rawaa *et al* who found that male to female ratio 14:1(8) which disagrees with chen*et al* who showed male: female ratio 3:1 (9) and this inconsistency might be attributed to low sample size of the

present study. Ankylosing spondylitis is a disease which occurs during the third decade of life (Rawaa, 2015), rarely at the age older than 45 year. About 10 -20 % of patients have the disease between 10 and 20 year of age (Chen, 2011). The mean age of the patients with AS in this study was 40.05 ± 8.02 years as shown in [Table-1], this result was nearly in accordance with previous study done on Iraqi AS patients by Rawaa *et al* that reported mean age of AS patient of 37.1±8.9 years (Rawaa, 2015), and other international study of Demirdal*et al* in AS Turkish patients that reported mean age of participated AS patient of 37.9±12.7 years (Sieper, 2013). In the current study we found that HLA-B27 was positive in 34(56.7 %) patients, and no subject from control group was positive and this difference is highly statistically significant (P-Value < 0.0001) and this is nearly in accordance with Al Attia *et al* that who found that the percentage to be 56% among Arabs in UAE (Al Attia, 2018). In the current study we found that there is a significant statistical difference of hs-CRP between positive and negative HLA B-27 groups (P-value=0.0437) in patients group which is in agreement with Freeston *et al* who found that AS patients have significantly longer disease duration if B27 positive, higher markers of disease activity, poorer functional status, poorer quality of life, and more extra-articular manifestations (Freeston, 2007). Studies have shown that TNF inhibitors improve health-related quality of life, patient-reported outcomes, anemia, C-reactive protein (CRP) levels, and sleep quality in patients with AS because TNF inhibitors control inflammation in the spine, as measured by various MRI sequences (Demirdal, 2013).

In the current study we found that mean serum level of hs-CRP higher in patients treated with conventional treatment, than in patients on biological treatment (infliximab infusion) and this difference is statistically significant (P-value = 0.0235) and these results were in accordance with other study done by Turina *et al* who found that hs-CRP is a useful biomarker of inflammation in this context as, despite not being elevated in all patients at baseline, it rapidly and significantly decrease in both axial and peripheral SpA treated with either infliximab or etanercept (Lin, 2012).

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Conflict of Interes: The authors declare no conflict of interest.

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