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Investigation of Cardiac Complications and their Incidence in Patients with Ankylosing Spondylitis

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ABSTRACT

Introduction: Ankylosing Spondylitis (AS) is a chronic inflammatory disease with unknown etiology which involves the sacroiliac and axial joints, but can also cause peripheral conflicts. It also comprises non-joint symptoms such as *acute anterior uveitis,* cardiac conduction defects, upper lobe pulmonary fibrosis, neurological involvement and renal amyloidosis. **Material and Methods:** This study was a cross-*sectional descriptive and analytical* survey. In this study, 50 patients with AS were examined according to the New York Criteria in Army 501 Hospital in Tehran. Physical examinations, laboratory testing and HLA-B27, as well as X-ray of the spine and sacroiliac *joint* were taken from all subjects and involvement grading was identified. The control group consisted of 40 healthy people with no evidence of disease. The people resembled the study group in terms of age, sex, smoking, presence of high blood pressure, history of ischemic heart disease and also diabetes. **Results:** The mean age of patients in control and study group was 33.97 and 33.65 years, respectively. 37 (92.5%) patients in the control group and 46 in study group (92%) were male. The mean duration of cardiac involvement in patients was 8.6 years with SD=6.26. In AS group, 48 (96%) patients suffered from back pain, 43 from enteritis, 100% from Ankylosing Spondylitis, one from unilateral involvement, 22(44%) from peripheral arthritis and 27 (54%) from HLA–B27.**Conclusion:** In total, Average heart involvement in the control group and AS group was 13.25 with SD=7.64 and 16.2 with SA=8.54, respectively, indicating no significant difference. In sum, based on the results obtained in this study, some types of heart involvements, such as mitral valve regurgitation and *Mitral* Valve Prolapse in AS patients are more prevalent than in the normal population.

Key words: Cardiac involvement, Mitral valve, Ankylosing Spondylitis, Arthritis.

1. INTRODUCTION

Ankylosing Spondylitis is an inflammatory disease with unknown etiology causing chronic inflammation of the joints and surrounding structures of the spine. The inflammation may lead to focal bone erosions and new bone formation. In this condition, there is a possibility of peripheral joint involvement and also, the development of inflammatory lesions in Non-articular organs such as eyes, heart, lungs, kidneys and digestive system (1, 2) .

The disease appears at young ages and predisposing family factors affect it and also there is a strong association with MHC genetic polymorphism (HLA-B27). The New York Criteria is used to diagnose Ankylosing Spondylitis in patients, so the same criteria has been used to classify Ankylosing Spondylitis in patients (3, 4). There is a significant correlation between the AS and histocompatibility antigens. Ankylosing Spondylitis disease affects men more than women (3:1) and the age of onset is typically from early

adolescence to age 35 and peak at age 28 (5, 6). Family history can be seen in 20-15% of cases and the risk for HLA-B_{27} positive is almost 20% (7). No specific reason has been found so far and no environmental factor such as bacterial pathogens has been defined for it. However, Klebsiella pneumonia has 6 amino acids similar to HLA-B_{27} and it seems that molecular mimicry is effective in its role in causing the disease (8-13). It should be noted that pathogenesis is not fully understood for AS, but it is almost certainly immune mediated (14-16).

Clinical symptoms of the disease are chronic back pain and stiffness which are typical early signs and start gradually. The pain in Ankylosing Spondylitis has inflammatory nature, so that appears in the morning and resting time and improves followed by activity (2, 14). Enteritis, especially plantar tendon problem, may exist which will lead to heel pain. The first unusual symptom in clinical examinations in Ankylosing Spondylitis is usually tenderness in sacroiliac joint or pain in the same area with hip hyperextension. Findings from long-term observations showed that in the long term, cases such as flattening the normal lumbar lordosis curve and limiting the movements in all lumbar spine planes are visible. When the disease progresses towards thoracic spine, chest expansion is limited (under 2.5 cm), resulting from cost vertebral joint fusion, and considering as a specific sign for AS, especially in young people (2, 14).

In addition to detailed clinical symptoms mentioned, some symptoms can be also seen in other organs and out of joint, such organs as eyes, lungs, kidneys, digestive system, nervous system and heart (2, 14, 17). Aortic insufficiency and variable degrees of atrioventricular block or branch block can be seen in approximately 5% of patients with a long period of illness. Less commonly, mitral insufficiency can be associated with aortic disease and almost all of the patients are HLA-B_{27} positive (18, 19). Valve involvement is histopathologically due to infiltration and accumulation of plasma cells and lymphocytes around the Vasa Vasorum, causing their lumen to be narrowed and the changes dilate and thicken the aortic root wall and shorten and thicken the aortic valve leaflets. Extension of inflammatory process and secondary fibrosis towards cardiac conduction system, namely, AV node and conduction branch proximal part, is the reason for conduction block (20-22).

In this study, the overall objectives are to investigate the frequency and type of cardiac involvement in patients referred to Army 501 Hospital, Tehran, and more specifically, frequency of cardiac involvement and complications in two groups of AS patients and healthy individuals, and finally comparing them and also examining the frequency of HLA-B_{27} and joint involvement in these patients.

2. MATERIALS AND METHODS

This study was a cross-sectional, descriptive-analytical survey, in which 50 patients with Ankylosing Spondylitis referred to Army 501 Hospital, Tehran, in 2001 - 2008 were compared with 40 healthy subjects as controls. This was a case-control study in which people with AS had been confirmed according to the New York Criteria. All patients, in addition to clinical examinations, underwent X-ray of the spine and sacroiliac joint. Also, all patients were referred to cardiologist to perform physical examination, electrocardiography and echocardiography during their visits. Control group was selected among healthy people having no signs of disease. The people were matched with the study group according to age, sex, smoking, high blood pressure, history of ischemic heart disease and also diabetes mellitus and finally referred to a cardiologist for electrocardiography and echocardiography. After collecting the information obtained and recording them, variables were analyzed using the software SPSS (Ver 15).

3. RESULTS

From total amount of patients in our sample, 50 AS patients were included in this study, 46 (92%) males and the remaining females. The control group consisted of 37 (92.5%) males and 3 (7.5%) females. The mean duration of disease in AS patients was 8.6 years, with 1 year minimum to 26 years maximum disease duration. The mean age of patients was reported 33.65 (SD=10.23) with age range of 20 to 63 years and age density between 20 to 40 years. In the control group, the mean age was 34 years (SD: 10.73) with minimum and maximum age of 20 and 63 years, respectively. Investigation of the frequency of HLA-B_{27} in patient group showed that 27 patients were HLA-B_{27} positive and 23 patients negative. Furthermore, the frequency of peripheral arthritis in the group indicated that 22 (44%) patients had peripheral arthritis and 28 (56%) were free of this complication. All AS patients had sacroiliac joint involvement, 49 (98%) bilateral and only 1 (2%) unilateral involvement. Based on back pain distribution, 48 (96%) patients had back pain and 2 (4%) were free of it.

P-Value	Control Group	Patient Group		
0.558	0	2	Number	Frequency of aortic stenosis
	0	4%	Percent	
0.606	2	3	Number	Frequency of aortic regurgitation
	5%	6%	Percent	
0.694	1	1	Number	Frequency of mitral stenosis
	2%	2%	Percent	
0.004	0	9	Number	Frequency of mitral regurgitation
	0	18%	Percent	
0.021	2	11	Number	Frequency of mitral valve prolapse
	5%	22%	Percent	
0.556	0	1	Number	Frequency of tricuspid valve stenosis,
	0	2%	Percent	
0.556	0	1	Number	Frequency of tricuspid valve regurgitation
	0	2%	Percent	
0.556	0	1	Number	Frequency of pulmonary valve stenosis
	0	2%	Percent	
0	0	1	Number	Frequency of pulmonary valve regurgitation
	0	0	Percent	

Table1: The frequency of different heart failure in AS patient and comparison with control group

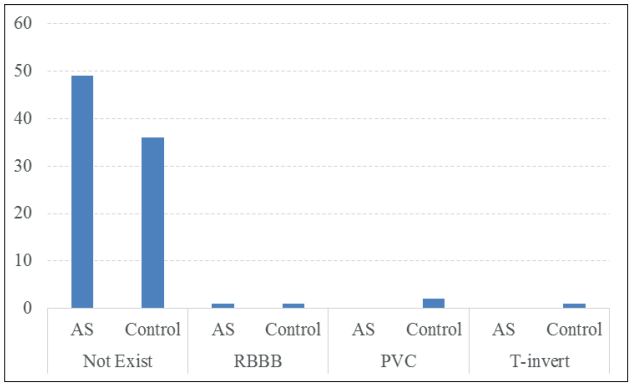

Figure 1. ECG changes in AS patients and controls

The frequency of different types of heart failure were studied, including aortic stenosis, aortic regurgitation, mitral stenosis, mitral regurgitation, mitral valve prolapse, tricuspid valve stenosis, tricuspid valve regurgitation, pulmonary valve stenosis and pulmonary valve regurgitation, that the results can be seen in Table 1.

ECG changes in both groups of AS patients and controls were studied. In patient group, 46 (98%) subjects had no changes and only 1 (2%) subject showed ECG changes in favor of RBBB who was HLA-B27 negative. In control group, 36 (90%) subjects unchanged and 4 (10%) had ECG change. The changes were RBBB in 1, PVC in 2 and T-invert in 1 (Figure 1).

Finally, since independent qualitative variable had two status (healthy group and AS patient group) and dependent variable was quantitative, T-test was used. Consequently, the average of this variable in AS patients and control group was 16.2±8.56 and 13.25±7.64. Because the significance level is P = 0.09 (>0.05), the main hypothesis is rejected, suggesting that being AS patient or healthy has no influence on cardiac involvement.

4. DISCUSSION

Ankylosing Spondylitis (AS) is a chronic inflammatory disease characterized by inflammation of the spinal cord and peripheral skeleton that can lead to local bone erosions or osteoporosis at the primary site. AS pathogenesis has not been fully recognized, but it is almost certainly immunity mediated. No laboratory test is diagnostic for AS. ESR and CRP are often high in most patients, but not always (23). Mild anemia may also be present. In severe cases, alkaline phosphatase level may also be high. On the other hand, in addition to peripheral joints and spine, other organs are also involved such as digestive system, lungs, eyes, kidneys, nervous system and heart. According to a recent study of AS patients, their cardiac involvement is divided into constructive involvement of heart itself including valves and vessels and cardiac conduction system. Valve involvements are as aortic or mitral insufficiency and conduction disorders as atrioventricular blocks or branch block that can be seen in approximately 5% of patients with long-term illness. Valve involvement is histopathologically due to infiltration of inflammatory cells, especially plasma cells and lymphocytes. Also, conduction disorders are led by inflammatory process and secondary fibrosis in conduction system. It is worth mentioning that cardiac involvement may be the first symptom in clinical examinations in AS patient and the patient refers with symptoms like pectoral angina, dyspnea, fatigue, syncope, followed by Stokes - Adams attack (2, 14, 19).

According to the results reported in detail in the results (table and graph), mitral valve regurgitation and its prolapse are the only findings with higher prevalence in AS patient than healthy controls and it is not true in other cases. It also seems that there is no logical relationship between AS diseases and cardiac complications due to the low number of subjects studied, and the incidence of cardiac complications had no significant difference in the patient and control groups (p=0.09).

Some studies have been already done on the relationship between heart failure and AS disease. 88 patients with AS underwent a physical examination, electrocardiography and echocardiography in Turkey. In this study, 5 out of 88 patients (5.7%) had some evidence of MVP, 6 (6.8%) mitral valve thickening without prolapse, 5 (5.7%) sever mitral regurgitation and 2 (2.3%) moderate aortic regurgitation that was lower than data obtained in the present study (24). Also, in another study conducted on 100 patients with AS in Bulgaria, statistical result of valvular disorders and conduction disorders was higher and lower than the present study, respectively (25). In one of the studies conducted in America, 44 patients with AS and 25 healthy subjects underwent clinical assessments and echocardiography. 82% of patients had aortic valve or root disease and in contrast, 27% of the control group had the same failure and valve regurgitation was observed in 50% of patients, that the data obtained in the control and patient groups was higher than the present study (26). In a study conducted by Brewerton et al., 5 out of 28 patients with AS suffered from more dilated left ventricle with poor muscle strength and early abnormalities in left ventricular diastolic were seen in echocardiography in 16 out of 28 patients with AS, who had been identified without cardiopulmonary symptoms and heart anomalies (27).

5. CONCLUSIONS

In conclusion, in total, according to data obtained in this study, it is suggested that the frequency of cardiac involvement in patients with AS doesn't differ with general population. But some of them, such as mitral valve regurgitation and mitral valve prolapse, had higher prevalence in AS patients than normal population in our study. It should be noted that minimal involvement of aortic valve observed in this study can be caused by a short period of illness, so that in other studies, the mean duration was 17-16 years, but in our study it was 8.6±6.26 years.

- **Author's contribution:** All authors contributed in all phases of preparing this article. Final proof reading was made by first author.
- **Conflict of interest: none declared.**

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