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The Pattern of Cardiovascular Manifestations in Egyptian Patients With Ankylosing Spondylitis and Its Relation to Disease Activity

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ABSTRACT

Background: Cardiovascular manifestations are one of the most common extraarticular features of ankylosing spondylitis (AS) patients. **Objective:** To characterize the cardiovascular symptoms of AS in a sample of Egyptian patients and to establish a connection between these symptoms and disease activity.

Patients and Methods: Forty adults with Spondyloarthritis (SpA) were chosen at random from Ain Shams University Hospital and diagnosed using Assessment of Spondyloarthritis International Society (ASAS) criteria for current cross-sectional study. All patients underwent detailed history taking, full clinical examination, laboratory investigations including (CBC, ESR, CRP, lipid profile) resting electrocardiogram, cardiac echo and carotid duplex to measure Carotid Intima-Media Thickness (CIMT), and evaluate disease activity using the Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-reactive protein.

Results: The majority of patients (about 66%) experienced cardiac symptoms have had a valvular lesion, with tricuspid regurgitation being the most common symptom (42.5%) then diastolic dysfunction (25%) followed by systolic dysfunction (20%), intra cardiac mass (5%) and pericardial effusion (2.5%). Most of our patients had abnormal lipid profile (hypertriglycerdemia 87.5%, hyperchlostremia in 80%, high LDL in 90%), 21 patients (52.5%) had abnormal CIMT. The ASDAS-CRP score of the patients was ranged from 0.4-4.6. It was statistically significant correlated with age, multiple cardiovascular lesions as systolic dysfunction, diastolic dysfunction ($p<0.05$), different forms arrhythmias, and CIMT ($p<0.05$) although there is no statistically significant link to lipid profile ($p>0.05$).

Conclusion: Cardiovascular affection in AS patients is frequent, whether being clinical or subclinical and it is related in a way to high disease activity.

Keywords: Cardiovascular manifestations, Ankylosing spondylitis, Lipid profile, Disease activity.

INTRODUCTION

Inflammatory illnesses of the sacroiliac (SI) joints and the rest of the axial skeleton are known as axial spondyloarthropathies (axSpA). Patients have a wide range of negative symptoms, including pain, exhaustion, restricted spinal motion, functional incapacity, and diminished mental health [(1)].

Chronic inflammatory back pain is a hallmark of axSpA, which can be subdivided into two categories based on clinical and radiological characteristics: A). Radiographic axSpA, which is characterised by radiographic and structural alterations in the SI joints. B) Sacroiliac inflammation revealed by MRI or the presence of HLA-B27 in combination with classic spondylarthritis characteristics are the gold standards for diagnosing non-radiographic axSpA[(2)].

In the United States, axSpA has an incidence of 0.9–1.4% among adults, which is comparable to that of rheumatoid arthritis [(3)].

AxSpA is often diagnosed and treated by rheumatologists. However, non-rheumatologists frequently miss the diagnosis because to a lengthy delay in making the determination [(4)].

One of the most prevalent extra articular symptoms of AS is cardiovascular system involvement, which is especially common in patients with long-term AS and peripheral joint involvement [(5)].

Different studies showed that those with AS have a higher chance of developing cardiovascular disease [(6)]. Atrioventricular (AV) block, aortitis of the ascending aorta, aortic insufficiency and branch block are all examples of cardiovascular involvement in AS. The most common problems are aortic insufficiency and conduction abnormalities. Although uncommon, mitral insufficiency in AS can lead to life-threatening heart failure [(7)].

The researchers in this study set out to do just that by identifying and analysing the cardiovascular symptoms of AS in a sample of Egyptian patients and determining how they relate to disease activity.

PATIENTS AND METHODS

Patients:

Forty adult patients were enrolled in the current cross-sectional study diagnosed with AS using the ASAS criteria [(8)]. From May 2021 through January 2022, patients from the Ain Shams University hospitals' outpatient clinic and the Internal Medicine and Rheumatology Departments were enrolled. Patients with psoriasis, inflammatory bowel diseases (Ulcerative colitis, Crohn's disease), other autoimmune diseases (SLE, RA, Scleroderma), diabetic, hypertensive, obese patients (metabolic syndrome), and hypothyroidism were excluded from the study.

Methods:

Clinical evaluation:

A complete history was taken from all subjects with focus on sex, age, duration of the disease, drug history as well as full clinical, and rheumatological examination with special emphasis on: axial spine (cervical, thoracic and lumbosacral regions) and examination of sacroiliac joints.

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Laboratory investigations

A set of laboratory tests were performed on each subject, including a C-reactive protein (CRP, mg/l), complete blood count (CBC), and measurements of total cholesterol, low density cholesterol (LDL-C), high density cholesterol (HDL-C), triglycerides, and erythrocyte sedimentation rate (ESR). (Low HDL-C has been defined as 40 mg/dL in men and 50 mg/dL in women; high LDL-C has been defined as a value > 160 mg/dL) Triglyceride levels (> 200 mg/dL) High total cholesterol (> 240 mg/dL)[9].

Disease activity assessment

The Ankylosing Spondylitis Disease Activity Score-C-reactive protein was used to quantify disease severity [10]. A score made of questions about pain on a scale from 0 to 10, back pain, peripheral pain/swelling, duration morning stiffness (0-10), patient global (0-10), CRP (A CRP value <2mg/l (0.2 mg/dl) is not allowed). Patients were assigned to one of five illness severity categories based on their ASDAS scores; ASDAS <1.3 it is referred as inactive disease; when ASDAS ranges from 1.3 to <2.1 it is referred as low disease activity; when ASDAS ranges from 2.1 to 3.5 it is referred as high disease activity, when ASDAS is >3.5 it is referred as a very high disease activity [11].

Imaging investigations

Echocardiography

The Philips iE33 echocardiographic device was used for all patient evaluations (Philips Medical Systems, Andover, MA, USA). Tissue Doppler imaging (TDI) mode was enabled on a phased array transducer covering the frequency range of 2.5 to 3.5 MHz. Transthoracic echocardiography (ECHO) performed by a single, blinded researcher in Ain Shams University's Cardiology Department.

Echocardiographic analysis

To assess the size and thickness of the left ventricle (LV), parasternal short-axis M-mode tracings were acquired under two-dimensional guidance. Disk summation was used to calculate the left ventricular (LV) ejection fraction (EF). An abnormal EF was defined by the American Society of Echocardiography (ASE) as 55% or below [12]. Diastolic left ventricular (LV) function was evaluated by measuring many Doppler parameters, including peak E velocity, peak A wave velocity, the E/A ratio, and the deceleration time of E velocity. Tissue Doppler imaging (TDI) was used to measure the E'-wave velocity in the lateral mitral annulus, and an E/E' ratio was subsequently determined [13]. The heart valves were analyzed using 2D, colour, and Doppler imaging.

Carotid artery duplex

A high-resolution vascular echo-graphic instrument and a linear electronic probe of 103 MHz are used (Philips Sonos 5500, Bothell, Washington, USA). All of our patients' carotid arteries were scanned with a 2D echo-color Doppler. Intimal medial thickness, the distance between the lumen-intima and the media adventitia of a blood vessel, was used as a proxy for the severity of atherosclerotic vascular disease in the carotid arteries (cutoff value equal or greater than 1.1 mm) [14]. The average reading was 0.74 ±0.14 mm [15].

For all patients, an electrocardiogram (ECG) was also recorded while they were at rest.

Ethical considerations:

This research followed the guidelines established by the World Medical Association in their Declaration of Helsinki. On September 17, 2020, the Ain Shams University Local Ethics Committee approved the study's protocol. This investigation has been assigned the reference number FWA000017585 by the committee. Acknowledgement of the risks and benefits of participation was documented by signed informed permission. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

We used MedCalc version 18.11.3 for data entry, processing, and statistical analysis (MedCalc, Ostend, Belgium). The statistical significance of a difference in a non-parametric variable was determined using Mann-Test Whitney's (U test). Analyzing the degree of connection between two numerical variables by correlation (using Spearman's approach). Correlation, often indicated by the symbol "r," describes the magnitude and direction of a linear relationship between two variables. Multiple-linear-regression analysis: As such, it was employed for determining the degree to which one quantitative variable depends on another group of factors. To evaluate ASDAS CRP's potential as a prediction tool, The ROC curve was analyzed. The area under the receiver operating characteristic curve (AUC) was read as: In this scale, scores of 0.9–1.0 are extraordinary, 0.8–0.89 are good, 0.7–0.79 are acceptable, 0.6–0.69 are poor, and 0.6 are an intolerable failure. The degree of specificity is typically expressed as a percentage. Here is the P-value, or degree of significance: "S" for significant (p 0.05), "HS" for highly significant (p 0.001).

RESULTS

Patients' demographic and clinical manifestations

The average age of the patients in the study was (41.3 ± 12.3) years, the majority (80%) of patients were males; while (20%) were females with ratio 4:1,and the mean disease duration was (14.5 ± 8.7) years, with (30%) of patients had positive family history. Regarding distribution of both articular and extra articular manifestations are presented in (Table 1). The ASDAS-CRP score might be anything between 0.6 and 4.6 with mean ± SD was 2.91 ± 1.23 as shown in table **1**.

Table (1): Distribution of demographic data, clinical manifestations, and disease activity score (ASDAS) among studied AS patients:

Demographic data		**Frequency (%) / Mean ± SD**
Age (years)		41.3 ± 12.3
Sex	Female	8 (20%)
	Male	32 (80%)
Disease duration (years)		14.5 ± 8.7
Family history (+ve)		12 (30%)
Articular manifestations		**Frequency (%)**
Axial involvement (Sacroiliitis and lumbosacral spine)		27 (67.5%)
Peripheral arthritis		21 (52.5%)
- Oligoarticular		13 (32.5%)
- Polyarticular		8 (20%)
Enthesitis		18 (45%)
Plantar fasciitis		16 (40%)
Dactylitis		4 (10%)
Extra articular manifestations		**Frequency (%)**
Eye involvement - Anterior uveitis		10 (25%)
Renal involvement - Proteinuria		2 (5%)
Lung involvement - Apical fibrosis		1 (2.5%)
Neurological involvement - Stroke (ischemic)		1 (2.5%)
ASDAS-CRP score	**Range**	0.6 – 4.6
	Mean± SD	2.91 ± 1.23

Lipid profile

Regarding lipid profile, our research showed that 87.5 percent (35 patients) had a triglyceride level (hypertriglyceridemia) and 80 percent (10 patients) had a Total Cholesterol level (hypercholesterolemia) (32 patients). Low level of HDL -C in 40% (16 patients) while abnormal level of LDL-C was in 90% (36 cases) (Fig. **1**).

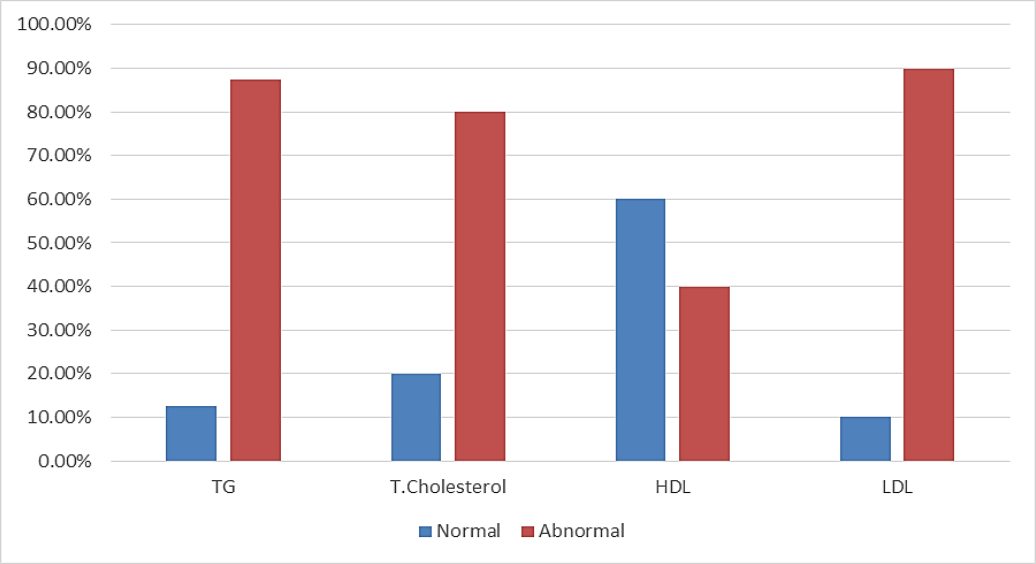

Figure (1): Distribution of lipid profile among studied AS patient

The cardiovascular Manifestations:

Left ventricular hypertrophy was the most common cardiac symptom, found in 30% of patients, according to an electrocardiogram, (20%) of patients had arrhythmia as follow; BBB (10%), first-degree AV block (7.5%), and third-degree AV block (2.5%), other findings were right ventricular hypertrophy (17.5%), left axis deviation (17.5%), and right axis deviation (2.5%). For ECHO Findings; (7.5%) of patients had MR, (42.5%) had TR, (2.5%) had PR, (12.5%) had AR, (5%) had segmental wall motion abnormality (SWMA) and intracardiac mass, (20%) had systolic dysfunction, (25%) had diastolic dysfunction, and (2.5%) had pericardial abnormality in the form of pericardial effusion. Regarding carotid artery duplex findings; the average CIMT was (0.83 ± 0.8) mm, with more than half of patients (52.5%), specifically increased intimal medial thickness, showed aberrant results.as shown in Table **2**.

Table (1): Distribution of ECG, ECHO and Carotid duplex findings among studied AS patients

ECG Findings		**Frequency**
Left ventricular hypertrophy (LVH)		12 (30%)
Arrhythmia:		8 (20%)
▪ **BBB:**		4 (10%)
- RT		3 (7.5%)
- LT		1 (2.5%)
▪ **AV block:**		4 (10%)
- First-degree		3 (7.5%)
- Third-degree (CHB)		1 (2.5%)
Right ventricular hypertrophy (RVH)		7 (17.5%)
Left axis deviation (LAD)		7 (17.5%)
Right axis deviation (RAD)		1 (2.5%)
ECHO Findings		**Frequency (%) / Mean ± SD**
EF (%) (N: 55-83)		58 ± 8.7
RVSP (mmHg) (N: 12.2- 57.4)		28.5 ± 4.9
Pulmonary artery pressure (mmHg) (N: <25)		22.2 ± 5.28
LVESD (mm) (N: 25- 41)		28.6 ± 3.67
LVEDD (mm) (N: 35- 56)		48.2 ± 4.6
Interventricular septum diameter (mm)		8.7 ± 1.25
Left atrial diameter (mm) (N: 20-40)		34.1 ± 5
Aortic root diameter (mm) (N: 20- 37)		39.6 ± 8.9
Right ventricular systolic diameter (mm) (N: 19.5- 31)		39.1 ± 9.31
Mitral valve	MR	3 (7.5%)
	MS	0 (0%)
Tricuspid valve	TR	17 (42.5%)
	TS	0 (0%)
Pulmonary valve	PR	1 (2.5%)
	PS	0 (0%)
Aortic valve	AR	5 (12.5%)
	AS	0 (0%)
SWMA	+ve	2 (5%)
Systolic dysfunction	+ve	8 (20%)
Diastolic dysfunction	+ve	10 (25%)
Intracardiac mass	+ve	2 (5%)
Pericardial abnormality "pericardial effusion"	+ve	1 (2.5%)
Carotid duplex Findings		**Frequency (%) / Mean ± SD**
Average CIMT (Rt + Lt) (mm)		0.83 ± 0.18
Right IM Thickness (mm)		0.83 ± 0.17
Left IM Thickness (mm)		0.83 ± 0.19
Abnormal (increased intimal mdial thickening)	+ve	21 (52.5%)

ECG: electrocardiogram. BBB: bundle branch block. RT: right. LT: left. AV: atrio-ventricular. CHB: complete heart block EF: ejection fraction. RVSP: right ventricular systolic pressure. LVESD: left ventricular end systolic diameter. LVEDD: left ventricular end diastolic diameter. MR: mitral regurge. MS: mitral stenosis. TR: tricuspid regurge. TS: tricuspid stenosis. PR: pulmonary regurge. PS: pulmonary stenosis. AR: aortic regurge. AS: aortic stenosis. SWMA: Segmental wall-motion abnormality CIMT: carotid intima media thickness. IM: intima media.

Association of cardiovascular manifestations with disease activity

Positive correlations between ASDAS-CRP and arrhythmia and left ventricular hypertrophy were found ($p < 0.01$). Heart dysfunction (both systolic and diastolic) was positively correlated with ASDAS-CRP score ($p < 0.05$), while non-significant correlation was found between lipid profile and ASDAS-CRP score ($p > 0.05$). Carotid duplex changes (abnormal CIMT) was significantly correlated to ASDAS-CRP score ($p < 0.05$) (Table **3**).

Table (3): Correlation analysis between lipid profile, ECG Findings and ECHO findings and ASDAS-CRP score

Lipid profile		**ASDAS-CRP score**	
		rho #	**P value**
TGs (mg/dL)		0.266	=0.0976
T. Cholesterol (mg/dL)		0.135	=0.4059
HDL (mg/dL)		-0.0653	=0.6891
LDL (mg/dL)		0.142	=0.3826
ECG Findings		**ASDAS-CRP score**	
		U ##	**P value**
Right ventricular hypertrophy	-ve	3.3 (1.4 – 3.7)	= 0.2324
	+ve	3.7 (3.5 – 3.9)	
Left ventricular hypertrophy	-ve	2.7 (1.3 – 3.6)	= 0.0081**
	+ve	3.7 (3.5 – 4)	
Right axis deviation	-ve	3.4 (1.5 – 3.7)	= 0.2246
	+ve	4.1 (4.1 – 4.1)	
Left axis deviation	-ve	3.3 (1.3 – 3.7)	= 0.3729
	+ve	3.5 (3.3 – 3.7)	
Arrhythmia	-ve	3.1 (1.3 – 3.7)	= 0.01*
	+ve	3.7 (3.5 – 4.4)	
- BBB	-ve	3.3 (1.4 – 3.7)	= 0.2144
	+ve	3.6 (3.4 – 4)	
- First-degree AV block	-ve	3.3 (1.4 – 3.7)	= 0.1359
	+ve	3.7 (3.5 – 4.3)	
- Third-degree AV block	-ve	3.4 (1.5 – 3.7)	= 0.0907
	+ve	4.6 (4.6 – 4.6)	
ECHO findings		**ASDAS-CRP score**	
		rho # / U ##	**P value**
EF (%)		-0.0237	=0.8847
RVSP (mmHg)		0.111	=0.4959
Pulmonary artery pressure (mmHg)		-0.216	=0.1801
LVESD (mm)		0.205	=0.2055
LVEDD (mm)		0.0875	=0.5912
Interventricular septum diameter (mm)		0.0534	=0.7436
Left atrial diameter (mm)		0.0632	=0.6984
Aortic root diameter (mm)		-0.0225	=0.8903
Right ventricular systolic diameter (mm)		-0.0608	=0.7092
Mitral regurge	-ve	3.3 (1.4 – 3.8)	= 0.7577
	+ve	3.5 (3.4 – 3.5)	
Tricuspid regurge	-ve	3.2 (1.4 – 3.6)	= 0.0706
	+ve	3.6 (2.8 – 4.1)	
Pulmonary regurge	-ve	3.4 (1.5 – 3.7)	= 0.8622
	+ve	3.3 (3.3 – 3.3)	
Aortic regurge	-ve	3.3 (1.4 – 3.7)	= 0.2964
	+ve	3.5 (3.3 – 3.8)	
SWMA	-ve	3.3 (1.5 – 3.8)	= 0.4942
	+ve	3.6 (3.5 – 3.7)	
Systolic dysfunction	-ve	3.2 (1.3 – 3.7)	= 0.026*
	+ve	3.8 (3.5 – 4)	
Diastolic dysfunction	-ve	3 (1.3 – 3.7)	= 0.01*
	+ve	3.7 (3.5 – 4.1)	

Lipid profile		ASDAS-CRP score	
		rho #	P value
Intracardiac mass	-ve	3.3 (1.5 – 3.8)	= 0.4942
	+ve	3.6 (3.5 – 3.7)	
Pericardial abnormality (pericardial effusion)	-ve	3.4 (1.5 – 3.7)	= 0.8622
	+ve	3.3 (3.3 – 3.3)	

(ASDAS)-CRP: The Ankylosing Spondylitis Disease Activity Score **rho:** Spearman's rho (correlation coefficient). TGs: triglycerides. T. chol: total cholesterol. HDL: high-density lipoprotein. LDL: low density lipoprotein **Mann-Whitney's U** test. M (IQR): median (inter-quartile range). ECG: electrocardiogram. BBB: bundle branch block. AV: atrio-ventricular. CHB: complete heart block M (IQR): median (inter-quartile range). EF: ejection fraction. RVSP: right ventricular systolic pressure. LVESD: left ventricular end systolic diameter. LVEDD: left ventricular end diastolic diameter. MR: mitral regurge. MS: mitral stenosis. TR: tricuspid regurge. TS: tricuspid stenosis. PR: pulmonary regurge. PS: pulmonary stenosis. AR: aortic regurge. AS: aortic stenosis. SWMA: Segmental wall-motion abnormality.
Note: P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS). *Significant test.

The association between cardiovascular symptoms and their respective independent predictors (demographic data, clinical, disease activity, laboratory factors) was evaluated using multivariate regression analysis shown in table (**4**).

Table (2): Multiple Logistic regression model for the Factors affecting cardiovascular manifestations occurrence using Enter method:

Predictor Factor	Aortic regurge (AR)		Tricuspid regurge (TR)		Arrhythmia		Atherosclerosis (CIMT)		Dyslipidemia	
	Coefficient	P value	Coefficient	P value	Coefficient	P value	Coefficient	P value	Coefficient	P value
Age	-1.29937	0.9999	-0.38169	0.2281	0.42782	0.9999	-1.2213	0.9999	-1.48615	0.9999
Sex "Female"	7.8967	0.9999	1.86082	0.3135	-9.45533	0.9999	-52.8467	0.9997	-36.0812	0.9995
Disease duration	**0.03729**	**0.021***	0.41941	0.2918	-0.17495	0.015*	1.98374	0.9999	9.1284	0.9995
Family history	30.9266	0.9998	**1.44036**	**0.049***	0.9999	1.0000	-43.9927	0.9998	-44.5784	0.9997
Sacroiliitis	21.1928	0.9998	-2.79046	0.2521	**2.40521**	**0.0099****	-63.2793	0.9997	-70.9966	0.9993
Pericard. Abnormal.	-75.6898	0.9996	23.77008	0.9987	-1.38598	1.0000	-62.6754	0.9998	-176.429	0.9992
Enthesitis	9.11046	1.0000	1.0572	0.6434	3.80318	0.9999	31.1713	0.9999	226.2603	0.9992
Dactylitis	29.21181	0.9999	-24.7427	0.9987	-6.43658	0.9999	-116.610	0.9997	-76.1974	0.9997
Plantar fasciitis	-14.2813	0.9999	0.17709	0.9210	7.21998	0.9998	-12.108	1.0000	-78.4593	0.9995
Neurol. Involve.	24.68755	0.9999	19.69050	0.9989	8.48917	0.9999	-92.7120	0.9997	-116.307	0.9998
Eye involve.	-36.25139	0.9998	0.34013	0.8818	19.58715	0.9999	54.3117	0.9994	-55.4619	0.9995
Lung involvement	76.12502	0.9998	16.2268	0.9991	-27.2916	0.9998	-68.828	0.9999	208.2596	0.9991
Renal involve.	-1.87276	1.0000	-25.4166	0.9981	31.3401	0.9997	6.33657	1.0000	-152.271	0.9988
Skin involvement	-32.67671	0.9999	26.14082	0.9986	12.72268	0.9999	92.39226	0.9995	6.88635	1.0000
Hb	-3.67368	0.9998	-0.25044	0.6885	-1.94136	0.9999	-15.6986	0.9995	-7.02536	0.9997
PLT	0.022659	1.0000	-0.00882	0.5139	-0.01107	1.0000	-0.5985	0.9998	-0.90523	0.9989
TLC	-0.070297	1.0000	-0.26340	0.4445	-2.69761	0.9998	11.8534	0.9995	-1.31127	0.9999
ESR	0.91572	0.9999	0.012824	0.8637	-0.28949	1.0000	0.11733	1.0000	**0.080435**	**0.021***
Uric acid	-3.94330	0.9999	-1.4912	0.2091	-3.6372	1.0000	50.1832	0.9989	4.06243	0.9999
TGs	-0.14553	0.9998	0.005623	0.5429	0.12636	0.9998	**0.013496**	**0.003****	---	---
T. Chol	0.098681	0.9999	-0.00387	0.7033	0.014323	1.0000	0.41592	0.9989	---	---
HDL	-0.37246	0.9999	-0.12953	0.2127	1.32467	0.9995	-2.05166	0.9995	---	---
LDL	0.12435	0.9999	-0.07112	0.0948	-0.13660	0.9999	-0.77416	0.9998	---	---
ASDAS-CRP score	-20.19739	0.9999	2.26962	0.1833	11.06315	0.9997	39.7889	0.9996	-37.7867	0.9993

Other factors excluded from the model as (p value > 0.1). OR: odds ratio. CI: confidence interval. Note: P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS).
*Significant test.

For determining the role of ASDAS-CRP score for prediction of cardiovascular manifestations among AS patients ROC curve was used, and the AUC was estimated. Cutoff values and performance characteristics are presented in table (**5**), Fig **2a**, **b**, **c**.

Table (5): Roc-curve of ASDAS-CRP score to predict cardiovascular manifestations

Variable	AUC	SE	Best Cut off point (Criterion)	Sensitivity (%)	Specificity (%)	P value
Aortic regurge (AR)	0.646	0.0920	>3.2	100	48.57	0.1133
Tricuspid regurge (TR)	0.669	0.0873	>3.5	52.94	73.91	0.0533
Arrhythmia	0.797	0.0746	>3.3	100	59.38	0.0001**
Atherosclerosis	0.752	0.0781	>3.4	66.67	73.68	0.0013**
Dyslipidemia	0.794	0.114	>1.3	88.57	80	0.01*

ROC (Receiver operating characteristic), AUC= Area under curve, SE= Standard Error.
Note: P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS).
*Significant test

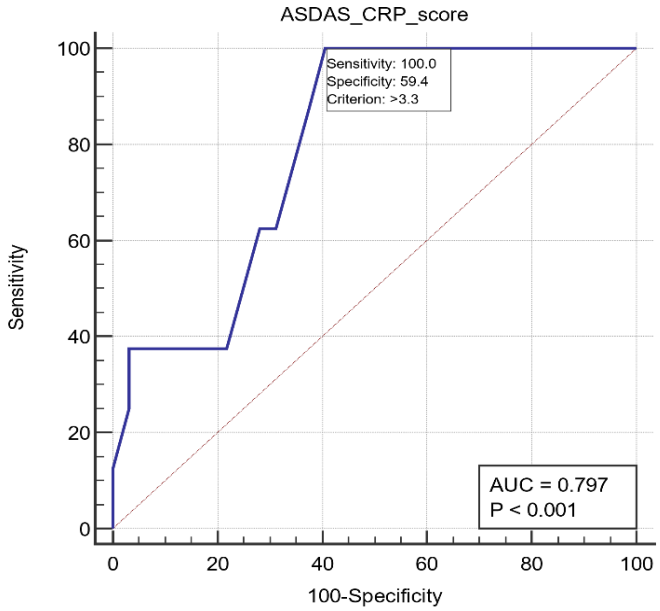

Figure (1): ASDAS-CRP score as a predictor of Arrhythmia.

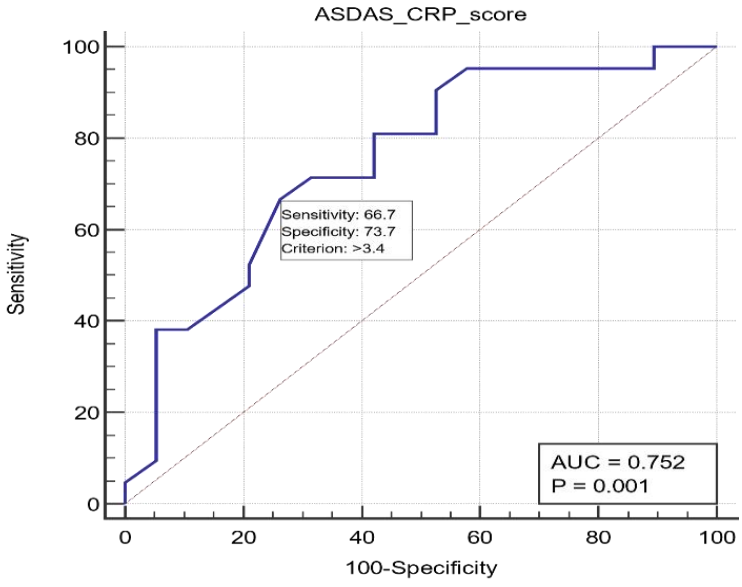

Figure (2b): ASDAS-CRP score as a predictor of Atherosclerosis.

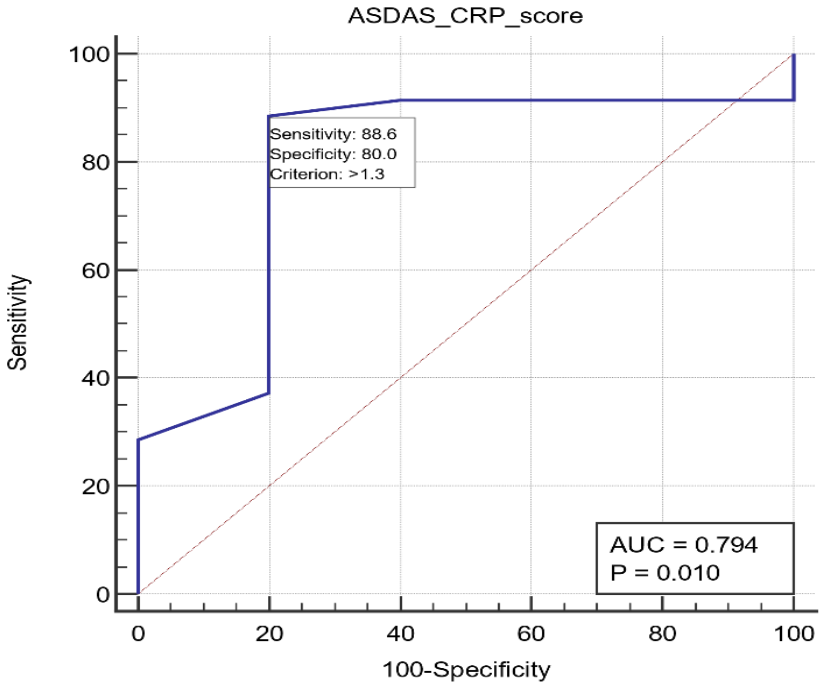

Figure (2c): ASDAS-CRP score as a predictor of Dyslipidemia.

DISCUSSION

The SI joints and the axial skeleton are the primary targets of AS, a chronic, multisystem inflammatory illness. Extra-articular organ involvement, enthesitis, and peripheral arthritis are also possible clinical symptoms [(16)].

Patients with chronic inflammatory disorders, such as AS, have a higher risk of cardiovascular (CV) disease, which is correlated with the inflammatory burden [(17)]. Therefore, the purpose of our study was to characterize the cardiovascular symptoms of AS in a cohort of Egyptian patients and to examine their relationship to disease activity.

In our study we found that patients mean age was (41.3 ± 12.3) years, and the mean disease duration was (14.5 ± 8.7) years. Patients were predominantly male (80%), with male: female ratio of 4:1; 30% of the population had a positive family history. That came in near concordance with **Ozkaramanli Gur *et al.*** [(18)] where, mean age of AS patients was (41.7±10.1) years while 62.7% male & 37.3% female with a ratio of (1.6:1). A relatively youthful study cohort with a short AS duration is reflected in the 5-year median symptom duration and the 10-year median time to diagnosis.

On the other hand, **Jeong *et al.*** [(19)] reported that, statistically, the average age of a patient's diagnosis was (32.2±12.2) years, (54.7% males &45.3% females) with male to female ratio was (1.2:1), Symptoms persisted for a median of 4 years, and only 16.5% of people had a history of SpA in their families. This previous difference could be explained by the different ethnicity and geographical distribution of the studied populations.

Regarding articular manifestations in our study the most frequent symptoms were axial skeleton affection in the form of sacroiliitis and lumbosacral spine (67.5%) followed by peripheral arthritis (52.5%) then enthesitis (45%) and lastly dactylitis (10%). This sequence of symptoms almost matches different studies [(20,21)].

In our study, among the several extra-articular symptoms experienced by AS patients, 25% experienced anterior uveitis. Our results were aligned with **Lindström *et al.*** [(22)], where 27% of their patients had history of anterior uveitis but chronic kidney disease seen only in 1% of the patients.

Regarding ECG findings, (7.5%) of patients had RBBB, (7.5%) had first-degree AV block, (2.5%) had LBBB, and (2.5%) had CHB, so our results showed that conductive abnormalities were the most prevalent arrhythmia among our patients. Different studies conducted on AS patients showed variable conduction abnormalities [(23,24)].

Regarding Echocardiography data; valvular affection was the most common findings as follow: TR in (42.5%), AR in (12.5%), MR in (7.5%), and PR was in only (2.5%) of patients.

These results came in agreement with different studies in which the most common ECHO abnormality in AS patients was valvular heart disease [(23, 24)]. The second most common finding by ECHO among our studied patients is diastolic dysfunction in (25%) of patients followed by systolic dysfunction in (20%) of patients, which came in agreement with **Almasi *et al.*** [(25)]. In contrary to our results, **Sorouch *et al.*** [(26)] demonstrated in their results that the frequency of

cardiac involvement in patients with AS doesn't differ with general population.

Regarding carotid duplex data in studied patients; the average CIMT was (0.83 ± 0.8) mm, with (52.5%) of patients had abnormal carotid thickness. The results were consistent with those of **Mishra *et al.* [27],** who found that the mean CIMT in AS patients was considerably greater than in the control group.

Contrary to our results, **Skare *et al.* [28]** compared CIMT scores of AS patients and controls and found no statistically significant differences. In their studies, they focused on groups with a mean age of 31.8±6.8 years could explain this difference.

It was shown that the ASDAS-CRP score was not significantly correlated with lipid profile variables ($p > 0.05$). Our result came in disagreement with **Berg *et al.* [29]** where the atherogenic lipids, TG and LDL-C, were significantly lower in patients with AS compared to controls.

Regarding electrocardiogram data, the ASDAS-CRP score was positively correlated with arrhythmia and left ventricular hypertrophy ($p < 0.01$). This came in agreement with **Bengtsson *et al.* [30]** who reported the association between ASDAS-CRP and conduction disturbance.

Systolic and diastolic dysfunction were both positively correlated with ASDAS-CRP score ($p < 0.05$). Our results came in concordance with **Min *et al.* [31]** where they found that very high ASDAS-CRP was associated with diastolic dysfunction and was one of the predictors of diastolic dysfunction in AS patient.

Correlation analysis showed a positive and statistically significant relationship between CIMT thickness and aberrant carotid thickness and ASDAS-CRP score ($p < 0.05$). Our results came in agreement with **Hatipsoylu *et al.*[32]** where correlated disease activity with acceleration of atherosclerosis [32]. In contrary to our results, **Silva & Costa [33]** found there is no linear relationship between ASDAS-CRP scores and CIMT measurements ($p = 0.932$, $r = -0.014$).

We used multivariate regression analysis to determine that there was a statistically significant relationship between the length of time someone had their condition and their risk of developing aortic regurge (AR) ($p = 0.02$). This finding comes in accordance with **Castañeda *et al.* [34]** who found that aortic valve disease prevalence increases with age and is especially related to the disease duration.

Contrarily, statistically significant differences were found between patients whose arrhythmia risk factors included a longer disease duration and those whose risk factors included sacroiliitis or a shorter duration of disease. ($p <0.05$). This findings disagrees with **Bengtsson *et al.* [30]** who reported that arrhythmia that result from intraventricular conduction disturbances is highly prevalent in AS, particularly in patients with long-standing disease duration.

Additionally, we found that the risk of atherosclerosis was significantly different between those with high TGs and those with low TGs. ($p < 0.01$), A statistically significant correlation was found between elevated ESR and an increased risk of developing dyslipidemia. ($p < 0.05$). **Verma *et al.* [35]** key indicators of accelerated atherosclerosis in AS, CIMT, are age, longer disease duration, higher disease activity (BASDAI and ASDAS), acute phase reactant, and proinflammatory cytokines (TNF-α).

CONCLUSION

Cardiovascular system involvement among ankylosing spondylitis patients is frequent, whether being clinical or subclinical and it is related in a way to high disease activity. Yet, it is still of question whether this involvement is a result of the chronic inflammatory state and lack of activity both resulting from uncontrolled disease only or another multifactorial pathogenesis are coexisting.

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