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RESEARCH ARTICLE

CARDIAC INVOLVEMENT IN IRAQI PATIENTS WITH SYSTEMIC SCLEROSIS (SCLERODERMA).

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Abstract

Background: Systemic sclerosis (Scleroderma) is a chronic multisystem disease of unknown etiology, has been considered a disease of metabolic disorder of connective tissue.

Methodology: A case control study. Thirty patients with systemic sclerosis forming the study group and twenty healthy individuals as a control group. Chest X-ray, electrocardiogram, and echocardiography were done for both groups for cardiac evaluation.

Results: The incidence of cardiac abnormality among patients group was (66.7%) in comparison to the control group (20%) (p = 0.001). Also there was an increase in the incidence of pericardial abnormalities (23.3%) and mitral valve thickening (33.3%) amongsclerodermic patients than control group (0%, 5%) respectively. There was a significant difference (P = 0.053) in the occurrence of cardiac involvement among diffuse scleroderma (75%) than limited one (33.3%).

Conclusion: Cardiac abnormalities affect more than half of patients with systemic sclerosis. These abnormalities appear to be more frequent in patients with diffuse scleroderma than in limited one.

Introduction:-

Systemic sclerosis (SSc) is a chronic multisystem disease of unknown etiology characterized by functional and structural abnormalities of small blood vessels, fibrosis of skin and internal organs, immune system activation and autoimmunity, (systemic sclerosis is rare in children, with a peak occurrence in individuals aged 35-65 years, female predominance is most pronounced, as ratio of women to men reach 7-12:1).Systemic sclerosis is classified into two subsets of disease, diffuse subset and a limited cutaneous subset by the degree of clinically involved skin[(1)].

Cardiac involvement in SSc is common, although, it is not often clinically manifested[(2)]; primary cardiac involvement is common in SSc being present in up to 50% of patients at post mortem[(3)].

Primary cardiac involvement in SSc may be manifested as pericardial disease, myocardial disease, conductive system abnormalities, or cardiac arrhythmias[(4)]. Pericardial involvement in SSc is often detected by histopathology and is usually silent, but not directly life threatening[(3)].

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Myocardial disease usually takes the form of congestive or dilated cardiomyopathy but sometimes may be restrictive[2].
Arrhythmias and conductive disturbances have long been recognized in SSc[4]. The cause of death related to cardiac involvement in sclerodermic patients usually results from intractable congestive heart failure, also arrhythmias are associated with increased mortality[3,5].

The prevalence of pericardial involvement in SSC on autopsy studies ranges from 33% to 71% and include fibrinous pericarditis, chronic fibrous pericarditis, pericardial adhesions and pericardial effusion[4].

Pathological studies have noted patchy myocardial fibrosis in 81% of patients with SSc[6], (this patchy fibrosis throughout the entire myocardium unrelated to coronary artery disease is characteristic of SSC, involvement of the myocardium is explained as areas of contraction-band necrosis are thought to occur as a consequence of hypoxia and/or reperfusion injury due to vasospasm of distal coronary vessels[1]).

Heart valves abnormalities have been variably reported in SSC; thickened mitral valves leaflets, verrucous lesion and aortic diseases have been reported but were of equal frequency in control population[3].

Diagnosis of cardiac involvement in patients with scleroderma should include a chest X-ray to determine size and shape of the heart, (it may show biventricular cardiac enlargement or show an enlarged triangle shaped heart consistent with pericardial effusion[3]).

Resting electrocardiographic abnormalities includes atrial and ventricular arrhythmias and conductive disturbances encountered in 50% of patients with SSc[6].

Echocardiography offers a non-invasive method of assessing cardiac chambers size, wall thickness and left ventricular systolic function in addition, it is a sensitive technique for the detection and semiquantification of pericardial effusion[7].

The aim of this study is to assess cardiac abnormalities in a sample of Iraqi patients with systemic sclerosis by using non-invasive cardiac techniques.

Patients and methods:
Thirty consecutive patients who fulfilled preliminary criteria of the American College of Rheumatology for definite systemic sclerosis were studied at the unit of Rheumatology in Baghdad Teaching Hospital during the period from July 2001 to July 2002.

Patients with previous rheumatic heart diseases, ischemic heart diseases and hypertension were not included in this study.

Twenty four patients were diagnosed as diffuse systemic sclerosis based upon the presence of skin involvement at least one area of the body beyond the face and fingers (i.e. forearm, upper arm or trunk).

The remaining 6 patients carried the diagnosis of limited scleroderma (CREST syndrome) in which subjects have 3 or more of syndrome's five signs (i.e. subcutaneous calcinosis, Raynaud's phenomenon,esophageal dysmotility,sclerodactyly and/or telangiectasias) with skin involvement limited to face and/or fingers.

Twenty healthy individuals approximately matched for age and sex were studied as a control group, a frill history and a systemic clinical examination was done on all patients and control group with special concentration on cardiovascular manifestations.

Patients with clinical evidence of the overlap syndrome or mixed connective tissue disease were excluded. Visceral involvement characteristic of diffuse scleroderma was evaluated either clinically or during investigations.

All patients were investigated for complete blood count, erythrocyte sedimentation rate (ESR), latex fixation test and antinuclearantibodies (ANA) done by indirect immunofluoresence assay and anticentromere antibodies (ACA) and antitopoisomerase (Anti SCL-70) antibodies done by an enzyme - linked immunosorbent assay (ELISA) method.

Twelve-leads electrocardiogram (ECG), CXR in P-A position and echocardiographic (Echo) examination by using (M-mode, 2-dimentionaldoppler echocardiography) were done for all the patients and the control group. Results of ECG, CXR and Echo findings were first analyzed by the same investigator.

A signed consent was obtained from all individuals in both groups for admission in this study.
Statistical analysis: The data were analyzed by using chi-square test for qualitative data and by student t-test for quantitative data, P-value of<0.05 was used as a level of significance.

Results:-

Subjects included in this prospective study were 30 patients with systemic sclerosis, 23 females and 7 males, their mean age was 35.8±11.2 years, and disease duration was 7.8±5.7 years.Twenty healthy individuals including 16 females and 4 males, their mean age 36.5± 9.2 years were studied as a control group.

Table-1 shows the selected characteristic features of 30 patients with systemic sclerosis.

Table-2 shows the nature and extent of cardiac abnormalities reported by Echo, ECG and CXR between sclerodermic patients and control group.

It was revealed that 20 out of 30 patients (66.7%) with SSc had at least one cardiac abnormality in comparison to the healthy control group 4 out of 20 individuals (20%) (p=0.001) which is statistically significant.

Echocardiographic findings:Variable cardiac findings were reported by echocardiography, some of which were significantly more frequent among systemic sclerosis than control group such as pericardial abnormalities (pericardial thickening and effusion) reported in 7 patients (23.3%) (P = 0.02); mitral valve thickening reported in 10 patients (33.3%) (P = 0.03).

While the difference in incidences of other cardiac abnormalities reported by echocardiography between SSc and healthy controls were small and statistically not significant (table 2).

Electrocardiographic findings:The incidence of cardiac abnormalities reported by ECG was significantly more frequent among SSc (23.3%) than control group (0%) (P=0.02), they included tachycardia, S-T segment depression and low voltage ECG but these abnormalities appear to be non-specific (table 2).

Chest X-rayfinding **:**The incidence of cardiac abnormalities reported by CXR in systemic sclerosis patients and healthy control group was little and statistically insignificant (table 2).

Table-3shows the difference in certain clinical and laboratory findings in patients with diffuse and limited scleroderma.

Some of these findings were significantly more frequent among diffuse scleroderma than limited type; such as cardiac involvement by (echocardiography, ECG and chest X-ray) reported in 75% (P=0.053), chest pain reported in 95.8% (P=0.003), palpitation reported in 83.3% (P=001), shortness of breath on exertion reported in 70.8% (P=0.01); Anti-SCL-70 antibodies detected in 83.3% (P=0.0001); mean ESR±SD detected in 40.70±23.23 (P=0.032).

The incidence of anticentromere antibodies (ACA) was significantly more frequent among limited scleroderma than diffuse type detected in (66.7%) (P=0.001).
While the difference in incidences of other clinical and laboratory findings between diffuse and limited scleroderma such as Echo, ECG, chestX-ray findings; ANA and pulmonary fibrosis by chest X-ray were little and statistically insignificant.

Table-4shows the difference in certain clinical and laboratory variables in sclerodennic patients with cardiac involvement and those without cardiac involvement.

Some of those variables were significantly more frequent among sclerodennic cardiac involvement than those without cardiac involvement such as mean disease duration 9.75±5.78 years (P=0.008); chest pain in 95% (P=0.053); pulmonary fibrosis in 35% (P:0.033) and anti SCL-70 Antibodies in 80% (P=0.03).

While there were no statistically significant association of sclerodennic cardiac involvement with patients age, gender, Rayanuds' phenomenon, palpitation, shortness of breath on exertion, ANA, ACA and ESR (P>0.05).

Table 1:-Selected characteristic features of 30 patients with systemic sclerosis

Patient characters	**Diffuse scleroderma (n=24)**		**Limited scleroderma (n=6)**		**Total (n=30)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Mean age (years)±SD	35.67±11.60		36.50±10.39		35.83±11.20	
Sex ratio (Female:Male)	3.8:1		2:1		3.3:1	
Mean disease duration±SD	8.26±5.96		6.25±4.60		7.86±5.70	
Rayanaud's phenomenon	22	91.7	6	100	28	93.3
Pulmonary fibrosis by (CXR)	7	29.2	0	0	7	23.3
Cardiomegaly by (CXR)	2	8.3	0	0	2	6.7
Small cardiac size by (CXR)	1	4.2	1	16.7	2	6.7
Chest pain	23	95.8	3	50.0	26	86.7
Palpitation	20	83.3	1	16.7	21	70.0
Shortness of breath onexertion	17	70.8	1	16.7	18	60.0
ANA present	20	83.3	4	66.7	24	80.0
ACA present	2	8.3	4	66.7	6	20.0
Anti SCL-70 Antibodies present	20	83.3	0	0	20	66.7

SD: Standard deviation, **CXR:** Chest X-ray, **ANA:** Antinuclear Antibodies,
ACA: Anticentromere Antibodies

Table 2:-The difference in prevalence of certain cardiac findings betweensclerodermic patients and healthy control group

Cardiac tests	**Diffuse scleroderma (n=24)**		**Limited scleroderma (n=6)**		**Total (n=30)**		**Control group (n=20)**		**P-value**
	No.	%	**No.**	**%**	**No.**	%	**No.**	%	
Echo-doppler positive findings									
Patients with at least one cardiac abnormality	18	75	2	33.3	20	66.7	4	20	0.001*
Pericardial abnormalities	6	25.1	1	16.7	7	23.3	0	0	0.02*
Mitral valve thickening	9	37.5	1	16.7	10	33.3	1	5	0.03*
Mitral valve prolapse	5	20.8	1	16.7	6	20.0	1	5	0.134
Mitral regurgitation	2	8.3	0	0	2	6.7	0	0	0 239
L.t atrial dilatation	1	4.2	0	0	1	3.3	0	0	0.409
R.t ventricular dilatation	0	0	1	16.7	1	3.3	0	0	0.409
L.t ventricular dilatation	2	8.3	0	0	2	6.7	2	10	0.57
Ventricular diastolic dysfunction	2	8.3	0	0	2	6.7	0	0	0.239
Septal wall thickening	1	4.2	0	0	1	3.3	0	0	0.409
T' cusp valve regurgitation	0	0	1	16.7	1	3.3	0	0	0.409
Total echo findings	16	66.7	2	33.3	18	'60	4	20	0.05*
ECG positive findings									
S-T segment depression	1	4.2	0	0	1	3.3	0	0	0.409
Tachycardia	2	8.3	0	0	2	6.7	0	0	0 239
Premature ventricular contraction	1	4.2	0	0	1	3.3	0	0	0.409
Low voltage	2	8.3	0	0	2	6.7	0	0	0 239

L.t Ant. Hemiblock	1	4.2	0	0	1	3.3	0	0	0.409
Total ECG findings	7	29.2	0	0	7	23.3	0	0	0.02*
Chest X-ray findings									
Cardiomegaly	2	8.3	0	0	2	6.7	0	0	0.239
Small cardiac size	1	4.2	1	16.7	2	6.7	0	0	0 239
Total chest X-ray finding	3	12.5	1	16.7	4	13.4	0	0	0.32

*significant

Table 3:-The difference in certain clinical and laboratory findings in patients with diffuse and limited scleroderma

Systemic sclerosis(n=30)					
Clinical and laboratory findings	**Diffuse scleroderma (n=24)**		**Limited scleroderma (n=6)**		**P-value**
	No.	**%**	**No.**	**%**	
Echocardiographicfindings	16	66.7	2	33.3	0.136
ECG findings	7	29.2	0	0	0.131
Chest X-ray findings	3	12.5	1	16.7	0 423
Cardiac involvement	18	75	2	33.3	0.053*
Chest pain	23	95.8	3	50	0.003*
Palpitation	20	83.3	1	16.7	0.001*
Shortness of breath on exertion	17	70.8	1	16.7	0.01*
Pulmonary fibrosis by (CXR)	7	29.2	0	0	0.131
ANA	20	83.3	4	66.7	0.36
ACA	2	8.3	4	66.7	0.001*
Anti SCL-70 Antibodies	20	83.3	0	0	0.0001*
Mean ESR±SD	40.70±23.23		18.67±9.63		0.032*
***** Significant					

Table 4:-The difference in certain clinical and laboratory variables insclerodermic patients with cardiac involvement and those withoutcardiac involvement

Systemic sclerosis(n=30)					
Clinical and laboratory variables	**With cardiac involvement (n=20)**		**Without cardiac involvement (n=10)**		**P-value**
	No.	%	**No.**	%	
Mean age (years)±SD	36.3±11.98		34.90±9.99		0.753
Mean disease duration ±SD	9.75±5.78		4.08±3.18		0.008*
Gender: Female Male	17 3	85 15	6 4	60 40	0.127
Rayanaud's phenomenon	18	90	10	100	0.301
Chest pain	19	95	7	70	0.053*
Palpitation	15	75	6	60	0.398
Shortness of breath on exertion	13	65	5	50	0.429
Pulmonary fibrosis	7	35	0	0	0.033*
ANA	18	90	6	60	0.21
ACA	4	20	2	20	0.999
Anti SCL-70 Antibodies	16	80	4	40	0.03*
Mean ESR±SD	38.80±25.07		31.40±17.98		0.414
* Significant					

Discussion:-

Weiss et al was the first to identify that the heart is a primary target organ in systemic sclerosis and described scleroderma heart disease as a distinct clinical entity in 1943[2,4].

Many subsequent studies have demonstrated the nature and the extent of cardiac involvement in systemic sclerosis; significant cardiac abnormalities are present in more than half of systemic sclerotic patients at autopsy, later non-invasive techniques like Echo and ECG have been developed for evaluation of cardiac involvement in systemic sclerosis, and now these non- invasive techniques are well established methods for detection and evaluation of cardiac involvement in systemic sclerosis[3,4,7,8].

In this study we aimed to evaluate the nature and the extent of cardiac involvement in a sample of Iraqi patients by using non-invasive cardiac techniques. The results from this study showed that the incidence of at least one cardiac abnormality in our sclerodennic patients was (66.7%) (P=0.001) in comparison to the control group (20%) which is comparable to other similar studies by Butrous et al[7], Badui et al[9], and Dubecq et al[10].

Also the study showed a significant increase in the incidence of pericardial abnonnalities (pericardial thickening and effusion) (23.3%) of sclerodermic patients in comparison to control group(0%) and this incidence is also comparable with incidence of pericardial abnormalities (15%-50%) reported by other echocardiographic studies[2,3,7,8], but it islower than the incidence of pericardial abnormalities reported at necropsy which was ranging from 33% to 72%[3,4]this could be explained as those non-invasive techniques were less sensitive in detection of mild cases of pericardial abnormalities.

The present study also revealed significant increase in the incidence of mitral valve thickening (33.3%) in comparison to the control group (5%) and this finding was comparable with the incidence of mitral valve thickening as reported by Riera et al[11]and Hata et al[12]studies.

Other findings reported by echocardiography in the current study, although they were increased in their incidence in comparison to the control group however this increment appears to be small and statistically insignificant, in contrast to other similar studies that demonstrated significant increment in Lt and Rt ventricular dilatation, Lt atrial dilation, ventricular diastolic dysfunction and mitral valve prolapse and regurgitation[2,8,13,14].

On the other hand, the current study showed an increase in the incidence of cardiac abnormalities reported by ECG among systemic sclerotic patients (23.3%) than control group(0%) (P=0.02) but these ECG findings appeared to be non-specific, this was comparable to similar findings reported in previous studies[3,7,15]. Chest X-ray findings in the present study were also not significantly different in both groups.

The present study showed significant differences in the incidence of cardiac involvement among diffuse scleroderma (75%) than limited one (33.3%) (P=0.053), this incidence was comparable with the incidences reported in previous studies[2,7,8,11,16].

The current study showed a significant direct correlation of chest pain, pulmonary fibrosis, longer disease duration and Anti SCL-70 Antibodies with sclerodermal cardiac involvement and this again is comparable with previous studies[4,10,17,18,19];while it is showing absence of such correlation with patients age, gender, Rayanouds' phenomenon, palpitation, ESR, ANA and Anticentromere Antibodies and this is also comparable with similar previous studies in sclerodennic patients without cardiac involvement[4,5,20,21,22].

Conclusion:-

Cardiac abnormalities affect more than half of patients with systemic sclerosis. These abnormalities appear to be more frequent in patients with diffuse scleroderma than in limited one. Electrocardiography and echocardiography can detect early changes in those patients.

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