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RESEARCH ARTICLE

ECHOCARDIOGRAPHIC EVALUATION OF CARDIAC DYSFUNCTION IN JUVENILE DERMATOMYOSITIS PATIENTS.

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Abstract

Background:- Cardiac involvement is common in adult polymyositis (PM) and dermatomyositis (DM). Similarly, pediatric patients with juvenile dermatomyositis (JDM) can be affected. Echocardiography is a valuable tool to assess cardiac dysfunction and to detect subtle signs of cardiac damage in these patients.

Objective:- The aim of this study was to assess left ventricular diastolic and systolic function in patients with JDM by echocardiography and to determine whether cardiac function and/or pathological ECG correlated with disease activity parameters.

Subjects and methods:- We evaluated 30 patients fulfilling the criteria for dermatomyositis including 7 males, and 23 females (6-27 years age) and compared them to thirty age and sex matched healthy control subjects (5.5-28 years age). Disease activity was measured by disease activity score (DAS) for JDM. Cumulative organ damage was measured by the Myositis Damage Index (MDI). A 12-channel electrocardiography (ECG) and echocardiographic assessment of conventional systolic and diastolic LV functions as well as tissue Doppler imaging (TDI). Long axis strain and E' were used to reflect systolic and diastolic function respectively.

Results:- Our results showed significant difference between patients and controls as regard pathological ECG findings (26.6% in patients vs 3.3% in controls) and it correlated with disease duration. Echocardiography of patients with juvenile JDM showed significant difference between patients and controls as regard long axis strain, E', and E/E'. There were no significant difference between patients and controls as regard other left ventricle dimensions and ejection fraction. Our results showed significant correlation between echocardiographic findings of systolic and diastolic dysfunction (long axis strain and E'), and clinical parameters including patient age, disease duration, DAS, MDI, prednisolone dose, and not with systolic blood pressure and CHAQ/HAQ.

Conclusion:- Patients with JDM showed subclinical systolic and diastolic cardiac dysfunction detected by echocardiography and this correlated well with disease activity.

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Introduction:-

Cardiac affection is well documented in inflammatory autoimmune diseases such as rheumatoid arthritis (RA) [1] and systemic lupus erythematosus (SLE) [2]. Cardiac involvement has been identified as the most important cause of morbidity and mortality in patients with dermatomyositis (DM). The increased cardiac mortality in patients with DM has been linked to congestive heart failure. Studies have demonstrated that congestive heart failure is the most

common cause of death, accounting for 21% of total cardiac mortality [3]. The underlying pathophysiological mechanisms that may cause cardiac manifestations involve myocarditis and coronary artery disease as well as involvement of the small vessels of the myocardium.

Juvenile dermatomyositis (JDM) is a disease of inflammation and vasculopathy[4]. Over the last few years, there have been several collaborative efforts focusing on how to assess the many aspects of juvenile dermatomyositis. It is possible that the myocardium in patients with JDM can be affected by inflammation, as seen in the adult form. The knowledge on cardiac manifestations in JDM has been scarce, only based on few studies [5], case reports [6] and clinical experience. Recently, one study on JDM have suggested that cardiovascular complications are rare [7]. One study reported that subclinical left ventricular dysfunction in JDM patients might have increased risk of developing clinical cardiac disease later in life, and thus might benefit from treatment aimed at reducing myocardial remodeling [8]. Another recent study reported that JDM patients had reduced heart rate variability, which was associated with elevated inflammatory markers, active disease and reduced myocardial function[9]. Doppler echocardiography is inexpensive, portable, and gives immediate feedback on cardiac structure, function, and flow.

The aim of this study was to assess cardiac function (systolic and diastolic) in patients with juvenile dermatomyositis, by echocardiography and to investigate abnormalities in ECG and to determine whether cardiac dysfunction and/or pathological ECG correlated with disease activity parameters.

Patients and methods:-

This case control study was done in Rheumatology& Rehabilitation, and Pediatrics departments, Faculty of Medicine, Zagazig University between May 2011 and May 2016.

The inclusion criteria were a probable or definitive diagnosis of DM according to the Bohan and Peter criteria for DM [10], disease onset before 18 years, minimum 24 months of disease duration and age ≥ 6 years at inclusion. We evaluated 30 patients fulfilling the inclusion criteria including 7 males, and 23 females with their age ranged from 6-27 years. Thirty age and sex matched control subjects were evaluated also with their age ranged from 5.5-28 years. Controls were apparently healthy volunteer subjects. We obtained informed consent from all patients and controls (and their parents if <16 years).

Exclusions; None of our patients was smoker, none had any other connective tissue diseases, such SLE, RA, overlap syndrome or mixed connective tissue disease. In addition, patients receiving pharmacological treatment (b-blockers, Ca channel blockers, diuretics, or other cardiac drugs) except for anti-rheumatic drug therapy were also excluded. None of the patients included in the study had evidence of hypertension, heart failure, coronary heart disease, diabetes mellitus, cardiac arrhythmias, valvular heart disease, or chronic renal failure (as assessed by history, physical examination, laboratory investigations and standard 12-lead ECG).

Clinical evaluation including medical history and physical examinations was performed for all subjects. The main laboratory measurements included triglyceride, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, serum uric acid, fasting blood glucose, anti-nuclear antibodies (ANAs), myositis specific antibodies, and muscle enzymes. Disease activity was measured by disease activity score (DAS) for JDM [11] (range 0–20), which consists of DAS skin (0–9) and DAS muscle (0–11). Cumulative organ damage was measured by the Myositis Damage Index (MDI, range 0–35/40), [12].

The Health Assessment Questionnaire (HAQ) [13] and the Child HAQ [14] were used to measure physical function in patients aged ≥ 18 years ($n=13$) and <18 years ($n=17$), respectively.

ECG and echocardiography:-

A 12-channel ECG was performed for patients and controls. ECG was classified, as normal, borderline or pathological. Criteria for borderline ECG were: incomplete right bundle branch block, severe sinus arrhythmia, STT changes or Sokalow criterion >35 mm. Standard criteria for pathological ECG were used [15].

Two-dimensional, M-mode and Doppler echocardiography were performed for all patients and controls using a Vivid 7 multidimension ultrasound scanner (GE Vingmed Ultrasound, Horten, Norway) using a 3 and 7 Mhz matrix probe [16]. Color coded Tissue Doppler was performed in patients and controls, with a frame rate of approximately 180.

Long axis strain and E' (early diastolic mitral annular tissue velocity), the most commonly used parameters reflecting left ventricular systolic and diastolic function respectively[17], were calculated.

Statistical analysis was performed using SPSS 16.0 for Windows (SPSS). Continuous data were analyzed by Student's t-test. Qualitative data are compared with chi-square test. Correlation between variables is performed using Spearman's rank correlation. The probability of error at 0.05 was considered significant, while at 0.01 and 0.001 was considered highly significant.

Results:-

Table (1) shows general and clinical characteristics of patients with juvenile dermatomyositis and controls. It showed nonsignificant difference between patients and controls as regard blood pressure and lipid profile. Table (2) shows ECG findings in patients with juvenile JDM and controls. It showed significant difference between patients and controls as regard pathological ECG findings [8 patients (26.6%) vs one control subject (3.3%)] and pathological / borderline ECG changes [10 patients (33.3%) vs 2 control subjects (6.6%)]. Table (3) shows echocardiography findings in patients with juvenile JDM and controls. It showed significant difference between patients and controls as regard long axis strain, E', and E/ E'. There were no significant difference between patients and controls as regard other left ventricle dimensions and ejection fraction. Table (4) showed correlations between echocardiographic findings and disease variables. It showed significant correlation between echocardiographic findings of systolic and diastolic dysfunction (long axis strain, E') and, clinical parameters including patient age, disease duration, DAS, MDI, prednisolone dose, and not with CHAQ/HAQ, and systolic blood pressure. Pathological ECG findings correlated only with disease duration(table 4).

Table 1:- Clinical features of patients with juvenile dermatomyositis and controls.

	Patients with JDM	Controls	test	p
Female/male	23(76.7/7(23.3)	21(70.0)/9(30.0)	.09	.77
Age , years	15.6+_4.6 6-27	16.1+_5.7 5.5-28	.87	.37
Body mass index, kg/m 2	20.1±2.7 18-24	21.5±3.3 19-25	1.49	.14
Disease variables; Duration from disease onset, years DAS score MDI CHAQ/HAQ Muscle weakness % Myalgia % Polyarthralgia % Heliotrope rash % Gottron sign % Raynaud phenomenon % Lung involvement % BP systolic, mm Hg (nonsig) BP diastolic, mm Hg (nonsig) Dyspnoea on exertion %	7(y) (4-16) 10.2±3.1(2-16) 13.3+_4.4(2-17) 1.75±0.9(0-2.9) 30(100.0) 18(60.0) 13(43.3) 22(73.3) 17(56.6) 5(16.6) 12(40) 111.5±7.5 (105-120) 71.4±3.5 (68-78) 5(16.6)			
Triglycerides (mg/dl) Total cholesterol(mg/dl) LDL cholesterol(mg/dl) HDL cholesterol(mg/dl) Fasting blood glucose(mg/dl) ANA-positive % Anti-Jo 1antibody positive %	150.57±49.6 185.62±61.87 104.56±53.72 53.75±19.34 81±14.4 17(56.6) 7(23.3)	141.71±54.91 181.75±58.01 100.54±61.87 52.98±19.35 86.4±12.6	.66 .79 .27 .18 1.43	.51 .26 .79 .86 .16
Antirheumatic medications; prednisolone Methotrexate Azathioprine	28(93.3) 22(73.3) 4(13.3)			

Values are number (%) or mean (SD), BP, blood pressure; CHAQ, Child Health Assessment Questionnaire; DAS, disease activity score; HAQ, Health Assessment Questionnaire; MDI, Myositis Damage Index; LDL, low density lipoprotein; HDL, high density lipoprotein; ANA, anti-nuclear antibody.

Table 2:- 12-channel electrocardiography (ECG) in patients with juvenile dermatomyositis and controls

	Patients with JDM	Controls	test	p Value
Pathological %	8(26.6)	1(3.3)	4.75	.03*
Pathological/borderline %	10(33.3)	2(6.6)	5.1	0.02*
PR, ms	137±12	142±11	1.52	.14
QRS, ms	90±10	92±5	.83	.41

Values are number (%) or mean (SD). PR, PR interval; QRS, QRS duration.

Table 3:- Echocardiography in patients with juvenile dermatomyositis and controls.

	Patients with JDM	Controls	p Value	Sig.
Two-dimensional echocardiography				
LA area, cm ²	14.3±3.6	15.8±3.9	1.57	.12
RA area, cm ²	13.6±3.2	13.8±3.7	.22	.82
LV ejection fraction, %	68±5.4	69.5±6.8	.95	.35
LV diastolic volume, cm ³	63±11.3	64.9±9.7	.69	.49
LV systolic volume, cm ³	21.7±5.6	22.1±4.6	.30	.76
M-mode echocardiography				
Septal diastolic thickness, mm	7.5±1.5	7.7±1.4	.53	.59
LV diastolic diameter, mm	44.8±5.3	43.9±5.0	.68	.50
LV systolic diameter, mm	28.1±4.0	26.8±4.6	1.17	.25
PW diastolic thickness, mm	8.3±2.2	8.4±1.7	.19	.85
Conventional Doppler				
E velocity, m/s	0.83±0.22	0.85±0.14	.42	.67
A velocity, m/s	0.50±0.15	0.48±0.19	.51	.61
E/A ratio	1.58±0.41	1.7±0.33	1.25	.22
MV deceleration time, ms	180±45	176±40	.36	.72
Tissue Doppler				
E' velocity, cm/s	12.6±2.5	14.9±3.2	3.10	.003*
E/E' ratio	9.7±1.3	6.1±1.1	5.12	0.001*
Long-axis strain	16.3±2.8	19.4±3.4	4.66	.00*

Values are mean(SD) ,LA; left atrium; RA; right atrium; MV; mitral valve; A, late diastolic transmitral flow; E, early diastolic transmitral flow; E', early diastolic tissue velocity; LV, left ventricle; PW, posterior wall.

Table 4:-Correlations between cardiac abnormalities and disease variables.

	Pathological ECG	Long axis	E'
Blood pressure systolic			
r	.22	.11	.15
p	.57	.85	.84
Age			
r	.39	.66	.54
p	.07	.00*	.04*
Disease duration			
r	-.62	-.82	-.76
p	.03*	.00*	.02*
DAS total			
r	.23	-.82	-.89
p	.53	.00*	.00*
MDI			
r	.10	-.48	-.90
p	.60	.04*	.00*
CHAQ/HAQ			
r	.17	.20	.09
p	.50	.53	.22
Prednisolone dose			
r	-.66	-.71	.53
p	.02*	.00*	.04*

BP, blood pressure; CHAQ, Child Health Assessment Questionnaire; DAS, disease activity score; E', early diastolic tissue velocity; HAQ, Health Assessment Questionnaire; MDI, Myositis Damage Index; r sp, Spearman correlation coefficient.

Discussion:-

In adult polymyositis and dermatomyositis, cardiac manifestations have been reported, but considered mainly subclinical [18]. Autopsy series of adult myositis have shown inflammatory changes in the myocardium; perivascular mononuclear cell infiltrates with or without small vessel disease and replacement fibrosis [19]. Few studies assessed the cardiac function in JDM patients until now.

In this study we assessed cardiac function; systolic and diastolic, in JDM patients by echocardiography for early detection and proper management of any cardiac dysfunction before possible irreversible damage. ECG was also performed for patients and controls.

Long-axis strain reflects the myocardium's ability to contract (systolic function), whereas E' reflects the stiffness of the myocardium and its ability to relax and recoil (diastolic function) [20]. We found reduced long-axis strain, suggestive of systolic dysfunction, in JDM patients, compared with controls (table 3). Systolic dysfunction can be explained by high cardiac muscle affection and disease activity associated with inflammatory mediators.

The cardiovascular affection in JDM does not seem related to lipid status [21]. Agreeing with the results of this study, we found non-significant difference between patients and controls as regard blood pressure and lipid profile (table 1). Lack of correlation with systolic blood pressure can be explained as none of our patients was hypertensive.

Our results agreed with one study that found systolic dysfunction in JDM by impaired long-axis LV strain, but interestingly not by ejection fraction, the more commonly used systolic parameter [21]. Lack of correlation of EF with most diseases and cardio-vascular parameters supports, that EF has limited value in detection of incipient heart failure as previously reported.

In this study, we found that E', suggestive of diastolic dysfunction, was reduced in patients with JDM compared to controls (table 3). This can be explained with slower relaxation of the affected myocardium of the left ventricle.

Our results agreed with one study that found that patients with JDM had lower E' and higher prevalence of pathological/borderline ECG than controls [8].

To explain these abnormalities, it is important also to correlate parameters of cardiac dysfunction with clinical manifestations and disease activity in patients included in our study. Interestingly, our results showed significant correlation between echocardiographic findings of systolic and diastolic dysfunction (long axis strain and E') and, clinical parameters including patient age, disease duration, DAS, MDI, prednisolone dose; and not with systolic blood pressure and HAQ/CHAQ. This correlation suggest that the myocardium in patients with JDM can be involved with time, and progress of the disease in parallel with skeletal muscle involvement in these young patients putting extra risk of severe cardiac sequelae.

These results were in agreement with a study that found that low E' and high E'/E' was predicted by 1 year DAS and correlated strongly with disease duration, and DAS total, muscle, and skin [8].

Our results showed that pathological ECG findings were detected in 8 JDM patients (26.6%) vs one control subjects only (3.3%) (table 2) but only correlated with disease duration, (table 4). These abnormalities can be related to damage of the conduction system by inflammation of the myocardium. This agreed with the results of Schwartz et al., 2011, although higher abnormalities were reported in adult polymyositis patients previously [22].

Conclusion:-

We found that JDM patients have subclinical systolic and diastolic dysfunction as well as more pathological ECG findings compared with controls. Both systolic and diastolic dysfunction were associated with long disease duration and high disease activity. This could suggest ongoing inflammation of the myocardium as found in the skin and muscle. Disease activity might increase the risk on the heart and thorough cardiological follow-up should be performed to identify and manage cardiac dysfunction as early as possible.

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