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## Asymptomatic Cardiac Involvement in Children with Systemic Lupus Erythematosus

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Cardiovascular involvement has been receiving increased attention in patients with Systemic Lupus Erythematosus (SLE). The aim of this study is to describe the cardiac involvement in children with SLE without overt cardiovascular manifestations mainly by echocardiography, in order to detect a very early impairment in cardiac function. Thirty children with SLE were diagnosed in the Collagen Vascular Disease Clinic of the New Children's Hospital, Cairo University were referred to the Pediatric Cardiology Clinic of the National Research Center. The study was done in a period between June to December 2005. Patients were subjected to full history taking and thorough clinical examination. Cardiac evaluation was done by plain chest X-ray, electrocardiography (ECG) and echocardiography with exclusion of patients with clinical evidence of cardiac disease, patients who have systemic hypertension and patients with history of rheumatic fever. Eighteen healthy children were included in the study as a control group. Echocardiographic examination revealed mild mitral regurge in 6 (20%) patients, moderate mitral regurge in 2 (6.6%) patients, mild tricuspid regurge in 8 (26.6%) patients and mild aortic regurge in 4(13.3%) patients. Eight (26.6%) patients had mild pulmonary hypertension ( $p = 0.001$ ), 6 (20%) patients had mild pericardial effusion and 8 (26.6%) patients had increased thickness of posterior wall and inter ventricular septum. ( $p = 0.001$ ). Indexes of left ventricular systolic and diastolic functions of SLE patients differed significantly from controls with reduced Ejection Fraction (EF) and Fractional Shortening (FS) as well as reduced peak early diastolic filling velocity (E) and ratio of early to late diastolic filling velocity (E/A). Deceleration Time (DT) and Pressure Half Time (PHT) were longer in the patients than controls. Late diastolic filling velocity (A) did not differ between patients and controls. We concluded that asymptomatic cardiac involvement in childhood systemic Lupus erythematosus is common. Early detection and treatment of cardiac abnormalities of SLE patients may lead to better survival. Therefore routine cardiac evaluation of children with SLE using ECG and echocardiography is recommended to detect silent cardiac involvement.

**Key words :** Systemic Lupus erythematosus, echocardiography, valvular regurgitation, pericardium, systolic function, diastolic function

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## INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an extraordinary complex autoimmune disease that touches on nearly all medical subspecialties (Dimitrios *et al.*, 1995).

Evidence from a broad range of basic science studies indicate that the pathogenesis of this disease is equally complex and may vary from patient to patient (Golbus and McCune, 1994).

The most common symptoms are constitutional complaints and joint or skin manifestations, renal disease and hypertension are also common at the time of presentation (Gunal *et al.*, 2003).

Cardiac involvement in patients with SLE has been described since the early 20th century. The frequency of cardiac manifestations has ranged from 4 to 78% in previous reports (Nihoyannopoulos *et al.*, 1990; Lehman, 1995). Complications may develop in all layers of the heart including the pericardium, endocardium, myocardium, valves, conduction system and coronary arteries, although frequently in a subclinical fashion (Iqbal *et al.*, 1999).

The aim of this study is to describe the cardiac involvement in children with SLE without overt cardiovascular manifestations mainly by echocardiography, in order to detect a very early impairment in cardiac function.

## PATIENTS AND METHODS

Thirty children with systemic Lupus erythematosus (SLE) diagnosed in the Collagen Vascular Disease Clinic of the New Children Hospital Cairo University were referred to the Pediatric Cardiology Clinic of the National Research Center. The study was done in a period between June to December 2005.

Patients were diagnosed fulfilling four or more of the American College of Rheumatology (ACR) classification criteria of SLE (Hochberg, 1997).

All patients were subjected to full history taking including the onset, duration of illness and thorough clinical examination. Laboratory findings at the time of presentation were obtained from clinical charts.

Cardiac evaluation was done by plain chest ray, electrocardiography (ECG) and echocardiography with exclusion of patients with clinical evidence of cardiac disease, patients who have systemic hypertension and patients with history of rheumatic fever.

Eighteen healthy children of the same age and sex were included in the study as a control group. Parental consent for all children were obtained.

**Echocardiographic examination:** Echocardiographic imaging was performed with vivid 3 machines-Norway equipped with 3 and 7 MHZ transducers. Two dimensional, Continuous Wave (CW), Pulse Wave (PW) and color flow Doppler examinations were done. The images were obtained according to the usual standardization (Takik *et al.*, 1978).

M-mode tracings were obtained, chamber dimensions and wall thickness were measured. The echocardiographic measurement were made in accordance with the norms suggested by the American Echocardiographic Society (Sahn *et al.*, 1978). Left ventricular hypertrophy was defined as left ventricular wall thickness of more than 12 mm in diastole. Left ventricular systolic function was determined and classified as mild, moderate and severe by measuring the Ejection Fraction (EF%) and fractional shortening (FS%) (Normal value: >60%, >28%), respectively (Gutgesell *et al.*, 1977).

Diastolic function of the left ventricle was evaluated by measuring peak early diastolic filling velocity (E), peak late diastolic filling velocity (A), E/A ratio, Deceleration Time (DT) and Pressure Half Time (PHT). Normal values for peak E and A velocities are  $0.91 \pm 0.11$  and  $0.49 \pm 0.08$  m/s, respectively. Normal values for E/A ratio and DT are  $1.9 \pm 0.4$  and  $199 \pm 32$  ms, respectively. Pressure Half Time (PHT) is less than 60 ms in normal populations (Kimball and Meyer, 2001).

In bidimensional images, mild pericardial effusion was defined as the presence of isolated posterior effusion, moderate pericardial effusion as the presence of anterior and posterior effusion and effusion of great magnitude as the presence of anterior, posterior effusion and abnormal excessive cardiac movements (Swimming heart) (Takik *et al.*, 1978).

Pulmonary Artery Systolic Pressure (PASP) was calculated and graded as mild, moderate and severe. (Marata *et al.*, 1997). Valvular functions were assessed, mitral and aortic regurgitation were graded using the criteria of Helmcke *et al.* (1987) and Perry *et al.* (1987), respectively.

**Statistical methods:** Statistical Package for Social Science (SPSS) program version 11 was used for analysis of data. Data were summarized as mean $\pm$ SD and percentage. Student's t-test for quantitative independent variables was used for analysis of difference between two groups. p-value is considered significant if less than 0.05.

## RESULTS

Demographic features of patients with SLE and controls. With no statistical significant difference are shown in Table 1.

Table 1: Demographic features of patients with SLE and controls

| Items                       | Patients                  | Controls                |
|-----------------------------|---------------------------|-------------------------|
| Number                      | 30                        | 18                      |
| Age (years)                 | (9 - 18)*                 | (8 - 16)*               |
| mean±SD                     | 14±2.017                  | 12.12±3.05              |
| Sex                         | 16 (53.3%) F-14 (46.6%) M | 8(26.6%) F-10 (33.3%) M |
| Duration of disease (years) | (1 - 10)*                 | -                       |
| mean±SD                     | 3.57±2.55                 | -                       |

SD: Standard deviation, SLE : Systemic Lupus erythematosus, M: Male, F: Female. \* : Minimum, maximum

Table 2: Clinical characteristics of SLE patients

| Clinical data             | No. of patients | Percentage (%) |
|---------------------------|-----------------|----------------|
| Mucocutaneous Involvement | 16              | 53.3           |
| Articular involvement     | 14              | 46.6           |
| Nephritis                 | 18              | 60.0           |
| Lesion of nervous system  | -               | -              |
| Anemia                    | 10              | 33.3           |
| Leukopenia                | 6               | 20.0           |
| ANA                       | 22              | 73.3           |
| Anti DNA                  | 16              | 33.3           |
| Use of corticosteroids    | 20              | 66.6           |
| Use of cytotoxics         | 14              | 46.6           |

ANA: Antinuclear antibodies

Table 3: Distribution of cardiac anomalies by clinical examination, electrocardiograph and echocardiography

| Items                                   | Cardiac anomalies    | Number (%) |
|-----------------------------------------|----------------------|------------|
| Clinical findings (left sternal border) | Mild systolic murmur | 2 (6.6)    |
|                                         | LAD                  | 4 (13.3)   |
| ECG findings                            | ST-T changes         | 4 (13.3)   |
| Echo findings                           | Mild MR              | 6 (20)     |
| - Mitral valve                          | Moderate MR          | 2 (6.6)    |
| - Tricuspid valve                       | Mild TR              | 8 (26.6)   |
| - Aortic valve                          | Mild AR              | 4 (13.3)   |
| - Pulmonary valve                       | -                    | -          |
| - PASP                                  | Mild PH              | 8 (26.6)   |
| - Pericardium                           | Mild effusion        | 6 (20)     |

ECG: Electrocardiography, LAD: Left Axis Deviation, MR: Mitral Regurge, TR: Tricuspid Regurge, AR: Aortic Regurge. PASP: Pulmonary Artery Systolic Pressure, PH: Pulmonary Hypertension

Nephritis was diagnosed by renal biopsy in 18 (60%) patients. All renal biopsy specimens showed a wide range of pathologic changes. According to WHO classification glomerular lesions were class IV in 4 (13.3%) patients, class III in 6 (20%) patients, class II A in 4 (13.3%) patients and class II B in 4 (13.3%) patients (Table 2).

The distribution of cardiac anomalies by clinical examination, electrocardiography (ECG) and echocardiography of SLE patients is represented in Table 3.

Figure 1 shows the Pulmonary Artery Systolic Pressure (PASP) of SLE patients in relation to controls. There is a highly significant increase in PASP of patients than controls ( $26.800 \pm 5.171 / 20.77 \pm 1.716$ , respectively  $p = 0.001$ )

Figure 2 illustrates the measurement of Posterior Wall (PW) and Interventricular Septum (IVS) of SLE patients in relation to controls. There is a highly significant increase

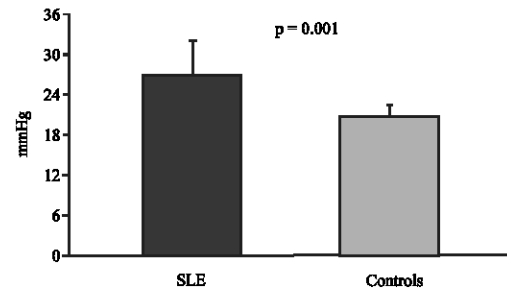


Fig. 1: Assessment of Pulmonary Artery Systolic Pressure (PASP) of Systemic Lupus Erythematosus (SLE) in relation to controls

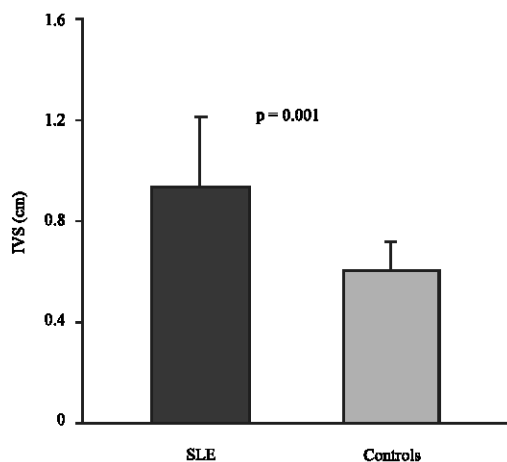
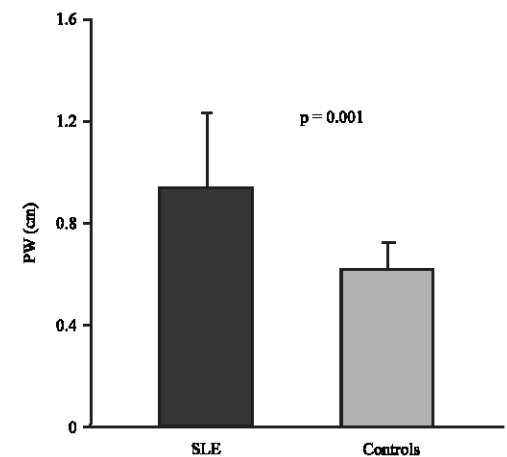


Fig. 2: Measurement of Posterior Wall (PW) and Interventricular Septum (IVS) of Systemic Lupus Erythematosus(SLE) in relation to controls

in the thickness of Posterior Wall (PW) in patients than controls ( $0.983 \pm 0.29 / 0.616 \pm 0.11$ , respectively,  $p = 0.001$ ) and highly significant increase in the thickness of Interventricular Septum (IVS) in patients than controls ( $0.942 \pm 0.27 / 0.605 \pm 0.11$ , respectively  $p < 0.001$ )

Table 4 shows the left ventricular diastolic filling parameters and systolic functions in patients with

Table 4: left ventricular diastolic filling parameters and systolic function in patients with SLE and controls

| Variables    | Patients<br>Mean±SD | Controls<br>Mean±SD | p-value |
|--------------|---------------------|---------------------|---------|
| E wave (m/s) | 0.717±0.11          | 0.923±0.17          | 0.05*   |
| A wave (m/s) | 0.496±0.74          | 0.514±0.07          | 0.5     |
| E/A ratio    | 1.15±0.29           | 1.697±0.175         | 0.05*   |
| DT (ms)      | 197.26±41.77        | 156.55±31.29        | 0.01*   |
| PHT (ms)     | 61.46±7.83          | 48.33±12.2          | 0.01*   |
| EF%          | 62.06±5.67          | 67.22±5.06          | 0.03*   |
| FS%          | 32.46±4.51          | 36.33±4.61          | 0.04*   |

DT: Deceleration Time, PHT: Pressure Half Time, EF: Ejection Fraction, FS: Fractional Shortening, \*p<0.05: Significant

SLE and controls. The EF, FS, peak E velocity and E/A ratio of the patients were significantly lower than controls.  $p = 0.03, 0.04$  and  $0.05$ , respectively DT and PHT were significantly prolonged than controls.  $p = 0.01$ , while A wave velocity did not differ between the 2 groups.

## DISCUSSION

Cardiovascular involvement has been receiving increased attention in patients with systemic Lupus erythematosus. Recent prospective studies using advanced diagnostic methods have allowed the delineation of the prevalence and significance of discrete cardiac manifestations such as valvular disease, myocardial dysfunction and pericardial disease (Dimitrios *et al.*, 1995).

In the present study we reviewed 30 children with SLE. The age of our patients ranged from 9-18 years, that agreed with the studies of Wallace *et al.* (1997), Iqbal *et al.* (1999) and Gunal *et al.* (2003) who found that the onset of SLE before the age of 5 years is rare.

The incidence of clinical renal disease was 60%, in our patients and the incidence of mucocutaneous, articular involvement and antinuclear antibodies (ANA) was 53.3, 46.6 and 73.3%, respectively.

In conjunction with our study Creso *et al.* (2002) reported the incidence of lupus nephritis, cutaneous, articular involvement and antinuclear antibodies was 72.9, 70, 60 and 90%, respectively and the lesion of nervous system was present in 32% patients while in our study no patients had nervous system lesion. Creso discussed that the childhood onset disease is usually associated with more severe organ involvement, nephritis, arthritis, malar rash are the most prominent presenting manifestations and auto antibodies are present in most cases.

In this study, 4 children had ECG changes (left axis deviation and ST-T segment changes). Similarly, Gunal *et al.* (2003) found in their study 6 cases had ST-T Segment changes. Guevera *et al.* (2001) reported that the most common ECG changes in SLE are nonspecific ST-T segment changes, arrhythmia and conduction disturbance.

Echocardiographic evaluation of our patients showed that the incidence of mitral, tricuspid and aortic regurge was 20, 26.6 and 13.3%, respectively. Kalke *et al.* (1998) found in prospective echocardiography study performed on 40 patients with SLE 17.1% patients had mitral regurge, 14.6% patients had aortic regurge and 7.3% patients had tricuspid regurge. Another study was done by Barton *et al.* (1999) on 21 SLE patients found that 19% had mitral regurge 14% had tricuspid regurge while no cases had aortic or pulmonary valve affection. The valvular affections are explained by Libman-Sacks endocarditis which is the most characteristic cardiac manifestation of the autoimmune disease systemic Lupus erythematosus. Libman and Sacks (1924) first published a description of these atypical, sterile, verrucous vegetations. Libman and Sacks (1924) endocarditis most commonly involves mitral and aortic valves, however all 4 cardiac valves and the endocardial surfaces can be involved. Valvular abnormalities are often clinically silent without significant valvular dysfunction. With the introduction of steroid therapy valvular thickening and regurgitation appear to occur more commonly with histologically active lesions identified less frequently, so the condition is not always recognized on echocardiographic images (Elizabeth and Elyse, 2004).

In the current study mild pericardial effusion was present in 20% of patients. In similarity to our results Gomcalves *et al.* (1998) found in a study on 24 SLE patients 21% had mild pericardial effusion. While Kalke *et al.* (1998) reported 12.2% patients with mild pericardial effusion. In both studies the effusion was asymptomatic.

Our patients showed 26.6% with mild pulmonary hypertension  $p = 0.001$ . Creso *et al.* (2002) found 21.4% of 70 patients with SLE had mild pulmonary hypertension  $p = 0.03$ . the pathogenesis of pulmonary hypertension in SLE has been related to vasospasm, Raynaud's phenomenon or to the lesion of vascular endothelium by antiphospholipid antibodies (Marata *et al.* 1997).

In the present study left ventricular wall thickness was increased in (26.6%) patients. This in agreement with Cujec *et al.* (1991), Barton *et al.* (1999) and Creso *et al.* (2002), who reported the incidence of increased wall thickness in SLE 14, 20 and 30%, respectively.

In the current study the EF and FS were decreased significantly than controls, this may be an early sign of impairment of left ventricular contractile function. Also left ventricular diastolic function indexes (peak E, E/A ratio, DT and PHT) were differed significantly than controls, this observation is an early manifestation of myocardial dysfunction. In conjunction with our results Gunal *et al.* (2003) found the indexes of left ventricular

systolic and diastolic function of their SLE patients differed from control (decreased EF, FS, peak E, E/A ratio and prolonged DT, PHT).

Several studies Giunta *et al.* (1993), Barton *et al.* (1999) and Astorri *et al.* (1997) reported the same results and concluded that abnormalities of systolic and diastolic left ventricular functions were common in SLE and progressive. Myocarditis is defined clinically as an inflammation of the heart muscle. Because patients with SLE can present with myocarditis (*Lupus myocarditis*). The immunopathologic changes in myocardium may be responsible for ultimate systolic and diastolic dysfunctions (Gunal *et al.*, 2003).

The present study has two limitations. First, the relatively small size of the patients group may prevent the detection of statistically powerful results. Secondly, longer follow up data which may provide information on further cardiac involvement or progressive myocardial impairment are not available yet. Studies with larger sample size and follow up will allow a more accurate estimation of the incidence of cardiac involvement.

## CONCLUSIONS

Asymptomatic cardiac involvement in childhood systemic Lupus erythematosus is common. Minor ECG abnormalities, valvular regurgitation, pericardial effusion, pulmonary hypertension, systolic and diastolic dysfunction are the common findings. Early detection and treatment of cardiac abnormalities in SLE patients may lead to better survival. Therefore routine cardiac evaluation of children with SLE using ECG and echocardiography is recommended to detect silent cardiac involvement.

## REFERENCES

- Astorri, E., P. Fiorina, E. Ridolo and G.A. Contini, 1997. Doppler echo cardiographic study of left ventricular function in patients with systemic Lupus erythematosus. *Cardiologia*, 42: 1179-1183.
- Barton, E.N., E.E. Chung, M.F. Smikle and Deceulaerk, 1999. Asymptomatic cardiac involvement in systemic Lupus erythematosus. *West Ind. Med. J.*, 44: 14-15.
- Creso, A.F., C.A. Izebel, H.C. Wilicam and L.B. Angela, 2002. Echocardiographic abnormalities and antiphospholipid antibodies in patients with systemic Lupus erythematosus. *Arq. Bras. Cardiol.*, 79: 1-14.
- Cujec, B., J. Sibley and M. Haga, 1991. Cardiac abnormalities in patients with systemic Lupus erythematosus. *Can. J. Cardiol.*, 7: 343-349.
- Dimitrios, T.B., A.A. Howard, J.F. Barri and E.B. James, 1995. Systemic Lupus erythematosus, emerging concepts. Part 1 Renal, neuropsychiatry, cardiovascular, pulmonary and hematological disease. *Ann. Intl. Med.*, 122: 940-950.
- Elizabeth, W.R. and F. Elyse, 2004. Libman-sacks endocarditis. Last up dated. *E Medicine*, 20: 1-11.
- Giunta, A., U. Picillo, S. Maione, S. Migliaresi and G. Valentine, 1993. Spectrum of Cardiac Involvement in Systemic Lupus Erythematosus: Echocardiographic, Echo-doppler Observations and Immunological Investigation. *Acta Cardiol.*, 48: 183-97.
- Golbus, J. and W.J. McCune, 1994. *Lupus nephritis*. Classification, prognosis, immunopathogenesis and treatment. *Rheum. Dis. Clin. North Am.* 20: 213-42.
- Gomcalves, L.M., J. Ribeiro, J. Isaac and A. Monteiro, 1998. Left ventricular filling in young patients with systemic Lupus erythematosus in stable phase. *Rev. Port Cardiol.*, 17: 27-33.
- Guevera, J.P., B.J. Clark and B.H. Athreya, 2001. Point prevalence of cardiac abnormalities in children with systemic Lupus erythematosus. *J. Rheumatol.*, 28: 854-859.
- Gunal, N., N. Kara, N. Akkok and N. Cakar, 2003. Cardiac abnormalities in children with systemic Lupus erythematosus. *Turkish J. Pediatrics*, 45: 1-5.
- Gutgesell, H.P. *et al.*, 1997. Evaluation of left ventricular size and function by echocardiography, results in normal children. *Circulation*, 56: 457.
- Helmcke, F., N.C. Nanda, M.C. Hsiung and B. Soto, 1987. Color doppler assessment of mitral regurgitation with orthogonal planes. *Circulation*, 75: 175-183.
- Hochberg, Mc., 1997. Updating the American college of rheumatology revised criteria for the classification of systemic Lupus erythematosus. *Arthritis Rheum.*, 40: 17-25.
- Iqbal, S., M.R. Sher and R.A. Good, 1999. Diversity in presenting manifestations of systemic Lupus erythematosus in children. *Pediatrics*, 134: 500-505.
- Kalke, S., C. Balakrishanan, G. Mangat and G. Mittal, 1998. Echocardiography and systemic Lupus erythematosus. *Lupus*, 7: 540-544.
- Kimball, T.R. and R.A. Meyer, 2001. Echocardiography. In: Moss and Adams Heart Disease in Infants, Children and Adolescents Allen, H.D. (Ed.), 6th Edn. Philadelphia lippincott Williams and Wilkins Co., 1: 252-262.
- Lehman, T.J., 1995. A practical guide to systemic Lupus erythematosus. *Pediatr. Clin. North Am.*, 42: 1223-1238.

- Libman, E. and B. Sacks, 1924. A hitherto undescribed form of valvular and mural endocarditis. *Arch. Intl. Med.*, 33: 701-737.
- Marata, I., K. Takenaka, S. Toshinoya *et al.*, 1997. Clinical evaluation of pulmonary hypertension in systemic sclerosis and related disorders. A Doppler echocardiographic study of 135 Japanese patients, *Chest*, 111: 63-43.
- Nihoyannopoulos, P., P.M. Gomez, J. Joshi and S. Loizous, 1990. Cardiac abnormalities in systemic Lupus erythematosus. Association with raised anticardiolipin antibodies. *Circulation*, 82: 369-275.
- Perry, G.J., F. Helmcke, N.C. Nanda and C. Byard, 1987. Evaluation of aortic insufficiency by Doppler color flow mapping. *J. Am. Coll. Cardiol.*, 9: 952-959.
- Sahn, D.J., A. DeMaria, J. Kisslo *et al.*, 1978. Recommendations regarding quantitation in M-mode echocardiography, result of a survey of echocardiographic measurement. *Circulation*, 58: 1072-1083.
- Takik, A.J., J.B. Seward and D.J. Hagler *et al.*, 1978. Two dimensional real-time ultrasonic imaging of the heart and great vessels-technique, image orientation, structure identification and validation. *Mayo Clin. Proc.*, 53: 271-303.
- Wallace, C., D. Schaller, H. Emery and R. Wedgwood, 1997. Prospective study of childhood systemic Lupus erythematosus. *Arthritis Rheum.*, 21: 599- 600.