The Journal of Tehran University Heart Center

Original Article

# Serum Uric Acid Correlation with Echocardiographic Indices in Children with Dilated Cardiomyopathy

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Received 23 April 2009; Accepted 28 August 2009

## Abstract

***Background:*** *Dilated cardiomyopathy (DCMP) is a myocardial disease characterized by dilated left ventricle or both ventricles and reduced contractility of the myocardium. In patients suffering from DCMP, the serum level of uric acid may increase. This research was designed to evaluate the effect of the serum level of uric acid on systolic and diastolic functions in patients with DCMP.*

***Methods:*** *This case-control study was performed on 30 patients with DCMP aged between 1 month and 12 years who were consistent with a control group in terms of age and gender. Patients suffering from congenital and acquired cardiac, renal, metabolic, endocrine, musculoskeletal, neurologic, vascular, and hematologic diseases were excluded. After physical examination, chest X-ray, and electrocardiography, systolic and diastolic parameters were measured via echocardiography, and fasting serum uric acid level was measured. The data were analyzed using the t-test and Pearson correlation coefficient.*

***Results:*** *The average age of the patients in the case and control groups was 7.28 and 7.13 years, respectively. There were 15 boys, and the rest were girls. The serum uric acid level in the case and control groups was 6.22 and 3.31 mg/dl, respectively; the difference was statistically significant (P value <0.01). There was a significant correlation between serum uric acid level and left ventricular isovolumic contraction, interventricular septal diameter, left ventricular septal diameter in diastole, and fractional shortening (P value <0.05).*

***Conclusion:*** *In children with DCMP, the serum level of uric acid increases significantly and this increase is significantly correlated with some of left heart echocardiographic parameters. This test is of predictive value for disease progression.*

*J Teh Univ Heart Ctr 4 (2009) 230-233*

***Keywords:*** *Echocardiography • Cardiomyopathy, dilated • Uric acid • Child*

## Introduction

Dilated cardiomyopathy (DCMP) is a disease characterized by the dilation of the left ventricle or both ventricles and reduced myocardial contractility.[1, 2] Although in many cases of DCMP no significant cause can be defined and they are thus termed idiopathic, DCMP can be induced by not only infectious diseases and especially viral diseases, but also by endocrine, metabolic, connective tissue, musculoskeletal, neurologic, hematologic, and coronary diseases as well as by malnutrition and drugs.[1-6] This disease can be diagnosed by chest X-ray, electrocardiography (ECG), echocardiography, and finally myocardial biopsy.

DCMP is manifested by cardiac failure. In patients with cardiac failure, renal uric acid excretion tends to increase as a result of a reduction in the glomerular filtration rate; and

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on the other hand, uric acid production increases secondary to endothelial damage, metabolic dysfunction, and increased activity of xanthine oxidase enzyme, which ultimately triggers a rise in the uric acid level.[1, 2]

Leyva and co-workers conducted a study in 1998, in which the circulating level of uric acid and inflammatory markers were measured in 39 male patients with congestive heart failure and 16 controls. They concluded that serum uric acid strongly correlated with circulating inflammatory markers in patients with congestive heart failure.[7] Cicoira and co-workers carried out a study on 150 adults suffering from congestive heart failure in 2002 and measured echocardiographic parameters and serum uric acid level. Their results showed that increased serum levels of uric acid correlated with diastolic heart dysfunction in patients with congestive heart failure and that xanthine oxidase inhibitors were theoretically effective in improving diastolic heart function.[8]

The present study was designed to determine the correlation between serum uric acid level and echocardiographic parameters in patients with DCMP.

## *Methods*

This case-control study, conducted over an 18-month period from March 2005, recruited 30 patients with confirmed DCMP admitted to the pediatric ward of our children's hospital. For each case, an age- and gender-matched healthy child with non-organic cardiac murmur was selected as a control. Children with congenital heart diseases and metabolic disorders as well those with endocrine, musculoskeletal, coronary artery, and hematologic diseases causing cardiomyopathy were excluded from the study. M-mode, two dimensional, and Doppler echocardiography were used to measure parameters such as isovolumic relaxation time (IRT), isovolumic contraction time (ICT), deceleration time (DT), peak E velocity (E), peak A velocity (A), E/A velocity ratio (E/A) , pre-ejection period (PEP), ejection time (ET), pre-ejection period/ejection time (PEP/ET), myocardial performance index (MPI), shortening fraction (SF), left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESSD), interventricular septal dimension in diastole (IVSD), interventricular septal dimension in systole (IVSS), left ventricular posterior wall dimension in diastole (LVPWD), and left ventricular posterior wall dimension in systole (LVPWS).

For each child, a questionnaire containing demographic characteristics and other parameters was completed. The data were analyzed using SPSS-14 software. For statistical analysis, descriptive statistics, t-test, and Pearson correlation coefficient were employed and a P value <0.05 was considered significant.

## *Results*

The results showed no significant difference between the average age of the case and control groups (7.28±2.06 and 7.13±1.97 years, respectively). The serum levels of uric acid in the cases and controls are shown in Table 1. Uric acid level was significantly higher in the case group than that in the control group (P value <0.0001).

Table 1. Serum level of uric acid (mg/dl) in case and control groups

| | Mean | SD | Min | Max | P value |
|---|---|---|---|---|---|
| Case | 6.22 | 1.53 | 4.5 | 10 | <0.0001 |
| Control | 3.31 | 0.92 | 2 | 4.5 | |

Table 2 depicts the right ventricle echocardiographic parameters in the case and control groups. The mean ICT, E, A, and E/A of the right ventricle in the case and control groups was not statistically different.

Table 2. Right-heart echocardiographic parameters in case and control groups

| Parameter | Mean±SD | P value | Parameter | Mean±SD | P value |
|---|---|---|---|---|---|
| IRT (ms) | | | E/A | | |
| Control | 96.20±11.58 | 0.0001 | Control | 1.39±0.30 | NS |
| Patient | 119.93±23.92 | | Patient | 1.43±0.49 | |
| ICT (ms) | | | PEP (ms) | | |
| Control | 30.26±21.28 | NS | Control | 76.03±7.97 | 0.0001 |
| Patient | 39.80±24.97 | | Patient | 97.66±15.84 | |
| DT (ms) | | | ET (ms) | | |
| Control | 119.70±18.48 | 0.0001 | Control | 264.00±23.79 | 0.0001 |
| Patient | 67.00±17.72 | | Patient | 227.20±32.83 | |
| E (cm/s) | | | PEP/ET | | |
| Control | 57.70±14.1 | NS | Control | 0.28±0.02 | 0.0001 |
| Patient | 62.66±19.35 | | Patient | 0.43±0.08 | |
| A (cm/s) | | | MPI | | |
| Control | 42.11±9.91 | NS | Control | 0.31±0.04 | 0.0001 |
| Patient | 46.21±14.01 | | Patient | 0.69±0.21 | |

IRT, Isovolumic relaxation time; ICT, Isovolumic contraction time; NS, Not significant; DT, Deceleration time; E, Peak E velocity; A, Peak A velocity; PEP, Pre-ejection period; ET, Ejection time; MPI, Myocardial performance index

Table 3 illustrates the left ventricle echocardiographic parameters in the case and control groups. The mean A, E/A, PEP/ET, IVSD, LVPWD, and IVSS of the left ventricle in the case and control groups was not statistically different.

Table 4 shows the correlation between the right-sided and left-sided echocardiographic parameters of the cases with their serum levels of uric acid. While there was no significant correlation between the right-sided echocardiographic parameters and the serum level of uric acid, left-sided SF, LVPWD, IVSD, and ICT parameters were significantly correlated with the serum level of uric acid.

Table 3. Left-heart echocardiographic parameters in case and control groups

| Parameter | Mean±SD | P value | Parameter | Mean±SD | P value | Parameter | Mean±SD | P value |
|---|---|---|---|---|---|---|---|---|
| IRT (ms) | | | PEP (ms) | | | IVSS (mm) | | |
| Control | 94.33±11.98 | 0.0001 | Control | 75.10±5.28 | 0.0001 | Control | 8.28±1.08 | 0.4142 |
| Patient | 113.53±18.01 | | Patient | 99.13±13.33 | | Patient | 8.65±2.18 | |
| ICT (ms) | | | ET (ms) | | | LVPWS (mm) | | |
| Control | 17.33±15.39 | 0.0091 | Control | 263.40±19.67 | 0.0001 | Control | 3.36±0.52 | 0.0190 |
| Patient | 31.60±24.41 | | Patient | 230.06±41.50 | | Patient | 3.85±0.97 | |
| DT (ms) | | | PEP/ET | | | EF (%) | | |
| Control | 120.90±15.45 | 0.0001 | Control | 0.35±0.39 | 0.2683 | Control | 63.60±5.60 | 0.0001 |
| Patient | 66.56±22.91 | | Patient | 0.44±0.09 | | Patient | 37.93±5.30 | |
| E (cm/s) | | | MPI | | | SF (%) | | |
| Control | 101.55±19.64 | 0.0042 | Control | 0.32±0.05 | 0.0001 | Control | 34.16±4.22 | 0.0001 |
| Patient | 84.77±23.10 | | Patient | 0.66±0.20 | | Patient | 26.13±7.55 | |
| A (cm/s) | | | IVSD (mm) | | | LVESD (mm) | | |
| Control | 57.54±15.81 | 0.1325 | Control | 5.43±0.88 | 0.7801 | Control | 21.56±3.22 | 0.0001 |
| Patient | 51.27±15.96 | | Patient | 6.07±1.73 | | Patient | 35.54±9.24 | |
| E/A | | | LVPWD (mm) | | | LVEDD (mm) | | |
| Control | 1.84±0.46 | 0.4940 | Control | 3.34±0.50 | 0.7203 | Control | 39.99±4.09 | 0.0001 |
| Patient | 0.50±1.75 | | Patient | 3.89±1.56 | | Patient | 47.95±8.99 | |

IRT, Isovolumic relaxation time; ICT, Isovolumic contraction time; DT, Deceleration time; E, Peak E velocity; A, Peak A velocity; PEP, Pre-ejection period; ET, Ejection time; MPI, Myocardial performance index; IVSD, Interventricular septal dimension in diastole; LVPWD, Left ventricular posterior wall dimension in diastole; IVSS, Interventricular septal dimension in systole; LVPWS, Left ventricular posterior wall dimension in systole; EF, Ejection fraction; SF, Shortening fraction; LVESD, Left ventricular end-systolic dimension; LVEDD, Left ventricular end-diastolic dimension

Table 4. Correlation between right-heart (RH) and left-heart (LH) echocardiographic parameters and uric acid levels in patients with dilated cardiomyopathy

| Parameters (N=30) | RH | P value | LH | P value |
|---|---|---|---|---|
| IRT (ms) | 0.09 | NS | 0.05 | NS |
| ICT (ms) | 0.21 | NS | 0.40 | 0.02 |
| DT (ms) | 0.10 | NS | 0.27 | NS |
| E (cm/s) | 0.11 | NS | 0.12 | NS |
| A (cm/s) | 0.14 | NS | 0.17 | NS |
| E/A | 0.91 | NS | 0.07 | NS |
| PEP (ms) | 0.35 | NS | 0.01 | NS |
| ET (ms) | 0.32 | NS | 0.11 | NS |
| PEP/ET | 0.05 | NS | 0.09 | NS |
| MPI | 0.05 | NS | 0.15 | NS |
| IVSD (mm) | - | - | 0.46 | 0.01 |
| LVPWD (mm) | - | - | 0.44 | 0.01 |
| IVSS (mm) | - | - | 0.34 | NS |
| LVPWS (mm) | - | - | 0.29 | NS |
| EF (%) | - | - | 0.30 | NS |
| SF (%) | - | - | 0.40 | 0.02 |
| LVESD (mm) | - | - | 0.31 | NS |
| LVEDD (mm) | - | - | 0.23 | NS |

IRT, Isovolumic relaxation time; ICT, Isovolumic contraction time; DT, Deceleration time; E, Peak E velocity; A, Peak A velocity; PEP, Pre-ejection period; ET, Ejection time; MPI, Myocardial performance index; IVSD, Interventricular septal dimension in diastole; LVPWD, Left ventricular posterior wall dimension in diastole; IVSS, Interventricular septal dimension in systole; LVPWS, Left ventricular posterior wall dimension in systole; EF, Ejection fraction; SF, Shortening fraction; LVESD, Left ventricular end-systolic dimension; LVEDD, Left ventricular end-diastolic dimension.

## *Discussion*

In our study, the serum level of uric acid showed a significant rise in the case group (P value=0.0001). Leyva and co-workers reported a 56.8% increase in uric acid in patients with chronic disease (P value<0.0001 ), which chimes in with our results.[9] The MPI of the right and left hearts of the case group was significantly different from that in the control group (P value<0.0001). The MPI of the left ventricle was statistically different between the case and control groups (P value<0.0001), as was the case in the Vaccari and Bossi study.[10, 11] Motaghi and co-workers had similar results in a study conducted in the Iranian city of Mashad.[12]

In the present study, the end-systolic dimension of the left ventricle increased significantly in the case group (P value<0.0001), and the difference between the end-diastolic volumes of the left ventricles was statistically significant in the case group when compared to those in the control group (P value<0.0001). The thickness of the posterior wall of the left ventricle differed significantly during systole between the case and control groups (P value=0.0190). The Kucuk study had the same findings on end-systolic and end-diastolic left ventricular thickness in the case and control groups.[13] In this study, right and left ventricular IRT differed significantly between the two groups (P value=0.0001), which is concordant with the results of the Noori and co-workers study, which reported that right and left ventricular IRT in the case group was higher than that

in the control group.[14] Although left ventricular ICT in our case group increased significantly when compared to that in the control group (P value=0.0091), there was no correlation between right ventricular ICT in the patients and controls (P value=0.1170); this particular finding was different from the Noori and co-workers study.[14] This dissimilarity could be due to the difference with respect to the mean age of the patients and also due to the fact that the Noori and co-workers study was performed on patients with thalassemia, in which both sides of the heart are involved (the right side normally precedes the left side). It is deserving of note that in patients with DCMP, this condition is reverse.

In our study, the serum level of uric acid in patients with DCMP was significantly correlated with the isovolumic contraction time of left heart, interventricular septum in diastole, left ventricular posterior septal wall thickness in diastole, and fractional shortening; no significant correlation was found with the other echocardiographic parameters. In another study by Cicoira and co-workers, it was shown that the serum level of uric acid had no correlation with end-systolic left ventricular volume and end-diastolic left ventricular volume, stroke volume, and ejection fraction. It should be stressed that the parameters included in our study were not assessed in the foregoing study.[8]

There is currently a paucity of data in the existing literature on serum uric acid level in children with DCMP; consequently, the inclusion of these parameters in the diagnosis, assessment, and prediction of the course of cardiomyopathy requires further investigation.

## Conclusion

Most of the indices studied in the DCMP group were impaired when compared with those in the control group, with the difference being statistically significant. In addition, our results demonstrated that although the left side of the heart is mainly involved in DCMP, the involvement of the right side should not be overlooked. The serum level of uric acid was significantly correlated with some echocardiographic indices such as left ventricular isovolumic contraction time, interventricular septum thickness in diastole, left ventricular posterior wall septum size in diastole, and shortening fraction. It can, therefore, be presumed that serum uric acid levels can be used for the diagnosis, assessment, and prediction of the outcome of DCMP or even maybe other cardiac diseases.

## Acknowledgment

This study was approved and was supported by the Research Center for Children and Adolescents' Health, Zahedan University of Medical Sciences. The authors would like to thank the staff and patients of the children's hospital of Zahedan and Hormozgan Universities for their kind cooperation. Many thanks are also due to Mrs. M. Kaykha and Mrs. Q. Salari for their help during the research process.

## References

1. Bernstein D. Disease of the myocardium. In: Behrman RE, Kliogman RM, Jenson HB, Stantone BF, eds. Nelson Text book of Pediatric. 18th ed. Philadelphia: WB Saunders Company; 2007. p. 1963-1972.
2. Olson TM, Hoffman TM, Chan DP. Dilated congestive cardiomyopathy. In: Moss AJ, Adams FH, eds. Heart Disease in Infant, Children and Adolescents. 7th ed. Philadelphia: Williams and Wilkins; 2008. p. 1195-1206.
3. Baboonian C, Treasure T. Meta-analysis of the association of enteroviruses with human heart disease. Heart Dec1997;78:539-543.
4. Caforio AL. Role of autoimmunity in dilated cardiomyopathy. Br Heart J 1994;72:530-534.
5. Grenier MA, Lipshultz SE. Epidemiology of anthracycline cardiotoxicity in children and adults. Semin Oncol 1998;25:72-85.
6. Kleinert S, Weintraub RG, Wilkinson JL, Chow CW. Myocarditis in children with dilated cardiomyopathy: incidence and outcome after dual therapy immunosuppression. J Heart Lung Transplant 1997;16:1248-1254.
7. Leyva F, Anker SD, Godsland IF, Teixeira M, Hellewell PG, Kox WJ, Poole-Wilson PA, Coats AJ. Uric acid in chronic heart failure: a marker of chronic inflammation. Eur Heart J 1998;19:1814-1822.
8. Cicoira M, Zanolla L, Rossi A, Golia G, Franceschini L, Brighetti G, Zeni P, Zardini P. Elevated serum uric acid levels are associated with diastolic dysfunction in patients with dilated cardiomyopathy. Am Heart J 2002;143:1107-1111.
9. Leyva F, Anker S, Swan JW, Godsland IF, Wingrove CS, Chua TP, Stevenson JC, Coats AJ. Serum uric acid as an index of impaired oxidative metabolism in chronic heart failure. Eur Heart J 1997;18:858-865.
10. Vaccari M, Crepaz R, Fortini M, Gamberini MR, Scarcia S, Pitscheider W, Bosi G. Left ventricular remodeling, systolic function, and diastolic function in young adults with Beta-thalassemia intermedia: a Doppler echocardiography study. Chest 2002;121:506-512.
11. Bosi G, Crepaz R, Gamberini MR, Fortini M, Scarcia S, Bonsante E, Pitscheider W, Vaccari M. Left ventricular remodelling, and systolic and diastolic function in young adults with beta thalassaemia major: a Doppler echocardiographic assessment and correlation with haematological data. Heart 2003;9:762-766.
12. Motaghi moghadam H, Alizadeh B. Assessment of cardiac function in children with thalassemia major with Doppler echocardiography and myocardiac prognostic index. Mash J Res Sci 2004;47:79-89.
13. Küçük NO, Aras G, Sipahi T, Ibiş E, Akar N, Soylu A, Erbay G. Evaluation of cardiac functions in patients with thalassemia major. Ann Nucl Med 1999;13:175-179.
14. Noori NM, Sohrevardi SR. Assessment of myocardial functional indices in children with thalassemia major referring to Ali Asghar hospital of Zahedan and comparison with control groups in 2003. Yazd Med Sci J 2004;12:56-63.