

Serum Uric Acid in Children with Dilated Cardiomyopathy in Basra: An Echocardiography Study

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Abstract: Background: Cardiomyopathy is primary myocardial disorders, are divided into dilated or congestive and non dilated or restrictive form. Echocardiography serves as a definitive tool for establishing the presence and type of cardiomyopathy. In patients with dilated type, the serum uric acid may increase, so the current research was designed to determine the level of serum uric acid and its correlation to systolic and diastolic function. **Method:** A case –control study has been conducted over a period of 24 months. Fifty four infants and children their ages ranged from 2-60 months, with confirmed dilated cardiomyopathy who were referred from pediatrics wards for echocardiographic examination were included. Other possible causes as: Metabolic, musculo-skeletal, coronary artery and hematological diseases were excluded. Fifty infants and children with normal physical and echocardiography reports were selected as control group; they were age and sex matched. Detailed echocardiographic examination was conducted to assess systolic, diastolic function and myocardial performance index and fasting serum uric acid was measured for all patients and the control group. **Results:** Age and sex distribution of the patients and control showed no significant difference reflecting the matching process. Mean serum uric acid in patients with dilated cardiomyopathy was $315.211 \pm 125.536 \mu\text{mg/L}$; significantly higher ($P=0.0001$) than the level in the control group (213.960 ± 77.016). Studied left ventricle echocardiographic parameters revealed that; deceleration time, myocardial performance index, ejection fraction, fractioning shortening and left ventricular end diastolic dimension were statistically significant in dilated cardiomyopathy patients compared to control group. Significant correlation between left sided echocardiographic parameters; ejection time, pre-ejection period /ejection time, myocardial performance index, interventricular septum dimension, stroke volume and serum uric acid were also documented. **Conclusion:** The level of serum uric acid increases in infants and children with dilated cardiomyopathy and correlates significantly with some left –heart echocardiographic parameters. So it has predictive value for progression of the disease.

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1. Introduction:

Cardiomyopathy, disease of the heart muscles dilated cardiomyopathy (DCM) is characterized by varying degrees of dilation of the ventricles, most predominantly the left ^(1, 2). The causes in the majority of pediatric patients are unknown (idiopathic dilated cardiomyopathy), but high proportion have either a genetic basis or are the sequel of viral myocarditis.

DCM is not only caused by viral infection, active myocarditis is identified in only minority of patients (2-15 %). ⁽²⁾ Patients with DCM may have other causes such as endocrine disorders as hypothyroidism, metabolic disorders as storage diseases, nutritional deficiency, exposure to cardiotoxic agents and systemic disorders such as connective tissue diseases. ^(1, 2)

Clinically in pediatric age groups, DCM is manifested by cardiac failure, the onset is usually insidious but sometimes symptoms occur suddenly. ⁽²⁾

Hyperuricaemia is a metabolic disorder frequently encountered in clinical practice, serum uric acid is elevated in 2-18% of population with age and sex reference values. Altered renal excretion of uric acid

causes hyperuricaemia but in many occasion the exact mechanism is not fully understood. ⁽³⁾

In patients with heart failure, renal uric acid excretion tend to increase as a result of reduction in glomerular filtration rate; as well as increase production of acid uric secondary to endothelial damage, metabolic dysfunction and increase activity of xanthin oxidase enzyme which triggers a rise in uric acid level. ^(1, 2)

Many researchers study hyperuricaemia as independent marker of impaired prognosis in heart failure. ⁽⁴⁾ Ciccoira et al carried out a study on 150 patients with congestive heart failure in 2002; they concluded that increase level of serum uric acid correlate with diastolic dysfunction. ⁽⁵⁾

So the current study was performed to determine the level of serum uric acid in children with DCM in comparison with control and its association to echographic parameters.

2. Methods

A case –control study has been conducted over a period of 24 months from the first of October 2013 till the end of September 2015.

Fifty four infants and children whose ages ranged from 2-60 months, with confirmed DCM; who were referred from pediatrics wards /Basra General Hospital for echocardiographic examination were included as cases in this study.

Children with cardiomyopathy due to other possible causes as: Metabolic, musculo-skeletal, coronary artery and hematological diseases were excluded. ⁽²⁾

In addition, fifty infants and children with normal echocardiography reports who were examined at the same period were selected as control group; they were age and sex matched.

An informed consent and agreement was obtained from the parents for recruitment in the study. A special examination information form was designed for the purpose of the study.

Detailed echocardiographic examination was conducted by a specialist pediatrician to assess

systolic, diastolic function and myocardial performance index. ⁽⁶⁾

Blood sample was aspirated and fasting serum uric was measured using COBAS INTGRA400 PLUS (Pediatric reference value is; (1-5) years is 100-350 μ mol). ⁽²⁾

Data were analyzed using SPSS software version 20 and expressed by mean \pm standard deviation (SD). Comparison was performed by using chi-square test and (ANOVA) test when appropriate.

3. Result

A total of 54 infants and children with DCM and 50 healthy children as control group were included in the study. Their ages ranged from 2-60 months and the mean was 26.61 \pm 17.45 for cases and 28.74 \pm 17.85 for controls. Age and sex distribution of the patients and controls shows no significant difference as shown in Table 1.

Table 1. Age and sex distribution of patients with DCM and control group

Variables		cases		Control group		P value
		No.(54)	%	No. (50)	%	
sex	male	26	(48.1)	28	(56)	NS
	female	28	(51.9)	22	(44)	
Age(Months)	Mean \pm SD	26.61 \pm 17.45		28.74 \pm 17.85		NS

Mean serum uric acid in patients with DCM is 315.211 \pm 125.536 μ mg/L; significantly higher than in the control group (213.960 \pm 77.016), (P<0.001) as shown in Table 2.

Table 2. Serum uric acid (μ mg/L) in patients with DCM and control group.

Serum uric acid	Mean	Std. Deviation	Minimum	Maximum	Median	Total	P value*
Cases	315.211	125.536	106.00	550.00	280.500	54	<0.001
control	213.960	77.016	106.00	465.00	196.000	50	

*ANOVA test

Studied left ventricle echocardiographic parameters revealed that; DT, MPI,EF,FS and LVESD are statistically significant in DCM patients than control group (Table 3).

Table 3. Left heart echocardiographic parameters in cases and control

Parameters*	Cases Mean \pm SD	Control group Mean \pm SD	P values
IRT(ms)	70.388 \pm 35.432	65.620 \pm 25.076	NS
ICT(ms)	64.870 \pm 35.711	58.200 \pm 38.667	NS
DT(ms)	111.314 \pm 37.027	126.580 \pm 34.550	<0.05
E/A(ms)	1.610 \pm 0.273	1.635 \pm 0.295	NS
PEP(ms)	112.107 \pm 52.001	106.616 \pm 55.389	NS
ET(ms)	117.888 \pm 53.625	196.200 \pm 53.423	NS
PEP/ET	0.709 \pm 0.418	0.619 \pm 0.438	NS
MPI	0.886 \pm 0.482	0.716 \pm 0.290	<0.05
IVSD(mm)	0.470 \pm 0.097	0.490 \pm 0.468	NS
LVPWD(mm)	0.458 \pm 0.178	0.472 \pm 0.340	NS
IVSS(mm)	0.541 \pm 0.111	0.570 \pm 0.103	NS
LVPWS(mm)	0.512 \pm 9.363	0.528 \pm 9.044	NS
EF (%)	48.624 \pm 16.645	56.580 \pm 13.853	P<0.01
FS (%)	25.018 \pm 9.567	29.300 \pm 8.741	P<0.05
LVESD(mm)	2.913 \pm 1.021	2.524 \pm 0.930	P<0.05
LVEDD(mm)	3.847 \pm 0.947	3.542 \pm 0.873	NS
SV	15.203 \pm 8.290	17.240 \pm 8.579	NS

*IRT, isovolemic relaxation time; ICT, isovolemic contraction time; DT, deceleration time; PEP, pre-ejection period; ET, ejection time; MPI, myocardial performance index; IVSD, inter ventricular septal dimension in diastole; LVPWD, left ventricular posterior wall dimension in diastole; IVSS, inter ventricular dimension in systole; LVPWS, left ventricular posterior wall dimension systole; EF, ejection fraction; FS, fraction shortening; LVESD, left ventricular end –systolic dimension; LVEDD, left ventricular end diastolic dimension.

In a bivariate correlation analysis, significant correlation between left sided echocardiographic parameters; ET, PEP/ET, MPI, IVSD, SV and serum uric acid while other parameters as IRT, ICT, E/A, PEP, LVPWD, IVSS, LVPWS, EF, FS, LVESD, LVEDD show no significant correlation as shown in Table 4.

Table 4: Correlation between serum uric acid and left heart echocardiographic parameters

parameters	P value
ET	0.044
PEP/ET	0.048
MPI	0.049
IVSD	0.015
SV	0.028

4. Discussion

The primary diagnostic features of DCM are left ventricular dilatation (LVD) and systolic dysfunction, LVD is ubiquitous for establishing the diagnosis.

The American Heart Association guideline for management of heart failure considers echocardiography as class I diagnostic test. Additionally Doppler imagining can provide valuable prognostic information.⁽⁶⁾ So the present study was designed to study left-heart echocardiographic parameters and its correlation to serum uric acid in patients with DCM and control group.

The current study revealed that serum uric acid significantly increased in patients with DCM than control group.

The association between hyperuricaemia and cardiomyopathy has been described by medical literatures. Hoepfer et al mentioned that elevated serum uric acid proved to be a common finding in patients with left-heart failure.⁽³⁾ As well as Leyva et al.⁽⁷⁾ It could be related to tissue hypoxia which is known to increase adenosine triphosphatodegradation⁽⁸⁾ and due to stimulation the expression of xanthine oxidase.⁽⁹⁾ On the other hand low cardiac output and venous congestion impaired glomerular filtration and tubular excretion of uric acid assuming to play a role.

Regarding echocardiographic parameters; the current study documented that myocardial performance index (MPI) was statistically significant in patients with DCM. Same result reported by Noori et al.⁽¹⁰⁾ Because MPI is reflecting global ventricular performance (normal value is 0.04), when increases it represents progressively worse performance. So it provides independent prognostic information in patients with heart failure due to cardiomyopathy.

Other parameters as deceleration time (DT), left ventricle end-systolic dimension (LVESD), ejection

fraction (EF) and fractioning shortening percent (FS %) were also statistically significant in patients with DCM.⁽¹⁰⁾

M-mode recorded to measure systolic dysfunction as ejection fraction and fractioning shortening is related to the prognosis. Short DT<130-150 ms; indicate a near-end diastolic dysfunction.⁽⁶⁾ A research conducted by Cicoira M. et al revealed that increased serum uric acid was associated with diastolic dysfunction.⁽⁵⁾

Significant correlation of Serum uric acid with ejection time (ET), pre-ejection period /ejection time (PEP/ET), myocardial performance index (MPI), inter ventricular septal dimension in diastole (IVSD), and stroke volume (SV).

Noori et al concluded significant correlation of serum uric acid and IVSD in addition to left ventricular posterior wall dimension in diastole (LVPWD) and fractioning shortening.⁽¹¹⁾

There is shortage of literatures concerning serum uric acid and pediatric DCM, so possibly the current studied parameters may aid in the assessment, diagnosis and prognosis of children with DCM.

Conclusion

Comparison of echocardiographic indices in patients with DCM and control group is statistically significant in certain indicators, although we study the left-heart indices the involvement of right-heart should not be ignored.

Correlation of serum uric acid with echocardiographic parameters such as ejection time (ET), pre-ejection period /ejection time (PEP/ET), myocardial performance index (MPI), inter ventricular septal dimension in diastole (IVSD), and systolic volume (SV) seems useful clinical and may be prognostic parameters. Therefore serum uric acid can be used as predictor of clinical diagnosis and assessment the severity and prognosis of DCM in pediatric age group.

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