THE ROLE OF CLINICAL AND INSTRUMENTAL METHODS IN EARLY DIAGNOSIS AND PROGNOSIS OF CARDIOMYOPATHY IN CHILDREN

D.I. Akhmedova, N.R. Akhmedova, D.M. Ruzmatova, S.B. Akhmedova
Republican Specialized Scientific-Practical Medical Center of Pediatrics of the
Ministry of Health of the Republic of Uzbekistan,
Tashkent Pediatric Medical Institute, Tashkent.

Abstract: Cardiomyopathy is a severe pathology, which requires careful study of clinical parameters and data of functional diagnostics methods (ECG, ECHO) for early detection. The study aimed to study the role of clinical and instrumental, biochemical, and immunological investigation methods for early detection and prognosis of cardiomyopathy course in children. Materials and methods of study: 85 children with cardiomyopathy under 18 years of age were examined, including 60 children with dilated cardiomyopathy (DCMP), 16 children with hypertrophic cardiomyopathy (HCMP) and 9 children with restriction cardiomyopathy (RCMP) who were hospitalized in the cardioreumatology department of the Republican Specialized Scientific-Practical Medical Center of Pediatrics of the Ministry of Health of the Republic of Uzbekistan. The control group consisted of 30 practically healthy children.

Keywords: children, cardiomyopathy, echocardiography, electrocardiography.

Introduction

In pediatrics, the issue of cardiovascular diseases (CVD) is one of the most important, due to the variety of clinical manifestations, difficulties in diagnosis and treatment, and the propensity to form the key risk factors for the development of cardiovascular events, which aggravate the long-term prognosis of the disease and reduce the quality of life and social adaptation.A special place among cardiovascular diseases is held by cardiomyopathies (cardiomyopathies), the growth of which has been noted recently, which is associated with the true increase in this pathology and the widespread introduction of highly informative instrumental methods of heart examination [1,2,3]. The frequency of sudden death among children with cardiomyopathy ranges from 1.5% to 4%, with arrhythmia being the cause of death in most cases. Heart rhythm disorders are both bradycardic (atrioventricular block) and tachycardic (unstable ventricular

tachycardia).The risk factors for sudden death include polymorphic ventricular extrasystoles. However, heart rhythm disorders are not an independent risk factor for sudden death, as they are closely associated with left ventricular dysfunction. There is a high frequency of ventricular fibrillation; its appearance is promoted by a sharp violation of the left ventricle's pumping function and increased pressure in its cavity [4,5,9]. Recently, technically sophisticated methods of heart and vascular imaging, such as computed tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI), including the introduction of a contrast agent, and some others have been developing intensively. However, their relatively low prevalence, cost, and difficulties in children (e.g., the need for anesthesia) limit their use on a large scale. As a result, electrocardiography (ECG) and echocardiography (echocardiography) remain the most common methods to study the cardiovascular system. The widespread introduction of highly informative instrumental methods for cardiac examination, primarily ehodopplercardiography, makes it possible to streamline the idea of cardiomyopathy as a nosological unit [3,8,10].

Considering the variability of the clinical picture of the IMP and its relationship to the severity of circulatory disorders, which depends on the degree of stagnation in a small and large circulatory circle where determines at the early stages of the signs of lesions of various parts of the heart as the severity of heart disease progresses is actual and relevant [6,7].

Based on the above, the purpose of this scientific study was to determine the role of clinical and instrumental, biochemical and immunological methods of research for early diagnosis and prognosis of cardiomyopathy in children.

RESEARCH MATERIALS AND METHODS

We examined 85 children with cardiomyopathy (CMP) aged up to 18 years, of which 60 children with dilated cardiomyopathy (DCMP), 16 children with hypertrophic cardiomyopathy (HCMP) and 9 children with restriction cardiomyopathy (RCMP) who were hospitalized in the cardioreumatology department of the Republican Specialized Scientific-Practical Medical Center of Pediatrics of the Ministry of Health of the Republic of Uzbekistan.

The diagnosis was made based on complaints, anamnesis data (obstetric anamnesis of the mother, anamnesis of life and diseases of the child, the transferred diseases, the nature of the current and duration of the disease), functional (ECG, EchoCG, Holter ECG monitoring), Biochemical (determination of cardio specific markers - creatine kinase, lactate dehydrogenase), immunological (cytokines - tumor necrosis factor-alpha (TNF),

IL-1, IL-6, IL-8,) and instrumental (chest X-ray, multispiral computer tomography) methods of examination.

ECG was carried out regularly to patients at each hospitalization in the cardioreumatology department, both at the primary examination and repeated hospitalization in the department on the Aplio-500 ultrasound machine ("Toshiba," Japan) with 3.0-6.5 MHz sector sensors. EchoCG was performed according to standard methods followinglocal and foreign guidelines and recommendations. Two-dimensional echocardiography with the determination of echometric parameters was used. Left ventricular myocardial contractility was estimated using the Teicholtz or Simpson ejection fraction (Ejection Fraction) and left ventricular myocardial shortening fraction (LV fraction) [6].

RESULTS AND THEIR DISCUSSION

The signs of cardiovascular insufficiency (CVI) observed in our patients are the clinical equivalent of left ventricular systolic dysfunction. The development and progression of cardiovascular insufficiency (CVI) are associated with reduced cardiac output (with systolic dysfunction) and stagnation of blood in the lungs and system veins above the weakened heart. These signs are concordant with the dynamics of the disease. Cardiovascular insufficiency manifested itself as a pronounced pallor of the skin with moderate oral cyanosis, the presence of wet wheezing in the lungs and shortness of breath. All signs of CVI in the form of pale skin, shortness of breath, moist wheezing in the lungs, and nasolabial triangle cyanosis were more common in children with all forms of CMP, and in children with DCMP, signs of CVI were more common, indicating a more severe course of DCMP in children. Children with CMP were categorized by clinical symptomatology (Table 1).

Table 1
Clinical indicators in children with CMP (%)

Symptoms	GCMP n=16 (%)	DCMP n=60 (%)	RCMP n=9 (%)	P	P_1	P_2
Tachycardia	12,5±8,3	91,6±3,6	11,1±10,5	<0,01	>0,05	<0,01
Weakened and spilled top shock	18,8±9,8	86,7±4,4	11,1±10,5	<0,01	>0,05	<0,01
Heart Boundary Expansion	75±10,8	100±0,00	22,2±13,9	<0,05	<0,01	<0,01
Weakening and deafness of the first tone	50±12,5	91,6±3,6	22,2±13,9	<0,01	<0,05	<0,01
Systolic noise	12,5±8,27	88,3±4,1	77,8±13,9	<0,01	<0,01	<0,01

Cardialgic syndrome	18,8±9,76	25±5,6	22,2±13,9			

Note: P is the validity of differences in rates between children with GCMP and children with DCMP; P_1 is the difference between indicators of children with GCMP and children with RCMP; P_2 is the difference between indicators of children with DCMPD and RCMP.

All sick children in the comparison groups had different degrees of cardiovascular insufficiency: I degree of CVI - 12.5±8.3% of children with GCMP. II A degree was found in greater numbers in children with GCMPs (30%). II B degree of CVI was higher among children with BCMP (36.6±6.2%). Signs of third-degree CNS were found in children with DCMP (33.3±6.1%) and children with RCMP (22.2±13.9%) (Table 2).

Table 2

Cardiovascular insufficiency rate in children with CMP

CVI degree	ChildrenwithGCMP n=16 (%)	ChildrenwithDCMP n=60 (%)	ChildrenwithRCMP n =9 (%)	P	P_1	P_2
CVI I	12,5±8,3	-	-	-	-	-
CVI II A	62,5±12,1	30±5,9	44,4±16,6	<0,01	<0,05	<0,05
CVI II Б	25±10,8	36,6±6,2	33,3±15,7	<0,05	>0,05	>0,05
CVI III	-	33,3±6,1	22,2±13,9	-	-	>0,05

Note: P is the validity of differences in rates between children with GCMP and children with DCMP; P_1 is the difference between rates of children with GCMP and children with RCMP; P_2 is the difference between rates of children with DCMP and children with RCMP.

According to the electrocardiographic study, signs of left ventricular hypertrophy were almost equally prevalent in children with DCMP (76.6±5.5%) and GCMP (75.0±10.8%); left atrial hypertrophy prevailed in children with RCMP (77.8±13.9%); isolated septal hypertrophy was typical only in children with GCMP and was found in 37.5% of children. Heart rhythm disturbances such as ventricular extrasystoles and sinus tachycardia prevailed in children with DCMP (33.3% and 50% respectively), and sinus bradycardia prevailed in children with GCMP (16.6% of children) (Table 3).

Detected dystrophic changes in the myocardium are more unfavorable in prognostic terms, leading to a decrease in myocardial function.

Table 3

Electrocardiographic indicators in children with CMP

Electrocardiographic indicators	ChildrenwithDCMP (n=60) (%)	ChildrenwithGCMP (n=16) (%)	ChildrenwithRCMP (n=9) (%)	P	P_1	P_2
Left ventricular hypertrophy signs	76,6±5,5	75±10,8	44,4±16,6	>0,05		
Left atrial hypertrophy signs	33,3±6,1	-	77,8±13,9	-	<0,01	-
Hypertrophy of ILF Signs	-	37,5±12,1	-	-	-	-
Incomplete blockage of right leg of Gis's bundle	10±3,9	25±10,8	22,2±13,9	>0,05	>0,05	>0,05
Total blockage of the left leg of the Gis's bundle	10±3,9	-	-	-	-	-
Ventricular extrasystoles	33,3±6,1	-	-	-	-	-
Sinus tachycardia	50±6,8	18,7±9,8	44,4±16, 6	<0,05	>0,05	<0,05
Sinus bradycardia	16,6±4,8	43,7±12,4	22,2±13,9	<0,05	>0,05	<0,05

Note: P is the validity of differences in scores between children with DCMP and children with GCMP; P_1 is the difference between children with DCMP and children with PCMP; P_2 is the difference between children with GCMP and children with RCMP.

X-ray examination revealed that heart size increase mainly due to leftwards in 66.7% of children with DCMP, total expansion was observed in 13.3% of children, the cardiothoracic index was 63.3±0.5% on average. Children with GCMPs had an average cardiothoracic index of 59.6±0.3%.

EchoCGs in children with CMP revealed: cardiac chamber expansion, systolic dysfunction with a 40% to 16% decrease in ejection fraction, and regurgitation on the mitral valve and tricuspid valve (Table 4).

Table 4.

Echocardiographic indicators in children with CMP

Echocardiographic indicators	ChildrenwithDCMP (n=60) %	ChildrenwithGCMP (n=16) %	ChildrenwithRCMP (n=9) %
Valve regurgitation (TC and MC)	60 (100%)	12 (75±10,8%)	9 (100%)
Systolic dysfunction	60 (100%)	-	-
Reduction of emission fraction below 40%	60 (100%)	-	-
LW wall hypokinesia	100%)	-	-
Paradoxical movements of the interventricular septum (IVS)	33,3±6,09%	-	-
Hypertrophy with dilatation	2 (3,3±2,32%)	2 (12,5±8,2%)	-
IVSwall hypertrophy	-	7 (43,75±12,4%)	-
Dilation of both atria or left atria	30 (50±6,4%)	6 (37,5±12,1%)	9 (100%)

Studies have shown that all echocardiographic disorders prevailed in children with DCMP compared to myocarditis. For example, all children diagnosed with DCMP had systolic dysfunction, a drop in ejection fraction below 40%, left ventricular wall hypokinesia, and valve regurgitation (MC and TC). Disturbances such as dilatation of both atria were found in children with RCMP. Hypertrophy of the walls on IVSwas observed only in children with GCMP (Picture 1).
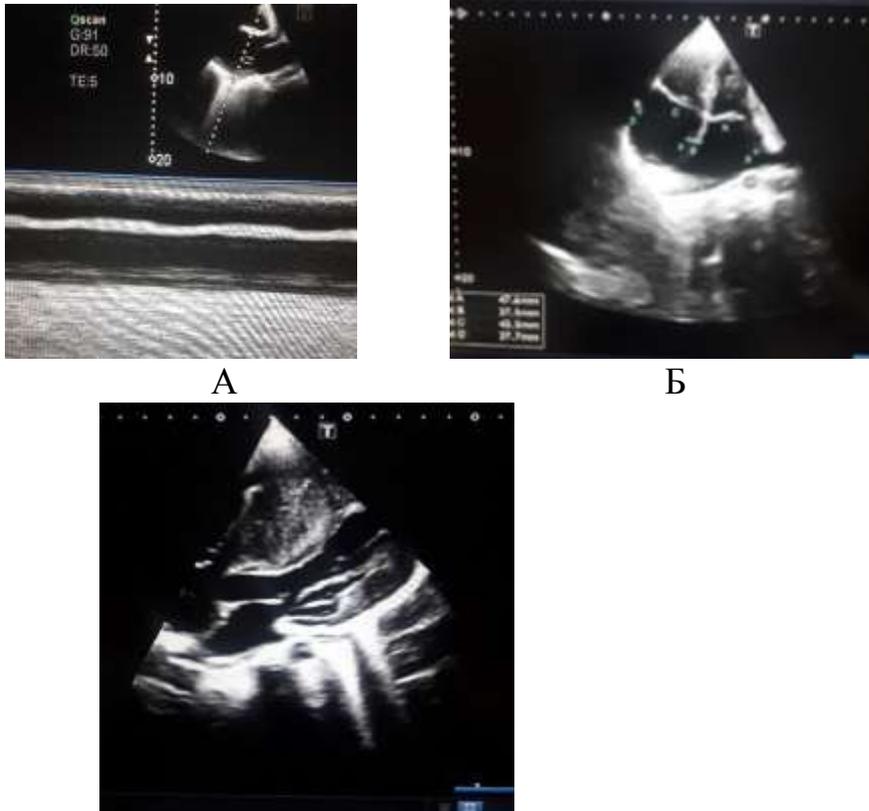
Fig.1. Echocardiogram in children with CMP. A - total hypokinesia of LV walls (Diagnosis: DCMP); B - dilatation of both atria (Diagnosis: RCMP); C-hypertrophy of interventricular septal walls (MVP) (Diagnosis: GCMP).

Much attention is paid to the search for objective parameters, which require the identification of cardiac markers in the blood to assess the existence of heart failure and measure its severity. Creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) were included in these parameters.

Table 5

Biochemical and immunological blood parameters in children with cardiomyopathy.

Biochemical markers	ChildrenwithDCMP	ChildrenwithGCMP	ChildrenwithRCMP
CPK(МЕ/л)	255,9±10,5	233,4±9,5	198±7,2
LDH(МЕ/л)	479,9±20,2	450,2±18,5	460±19,8
IL-1 (пг/мл)	1,98±0,02	1,8±0,02	1,5±0,04
IL-6	6,8±0,5	2,8±0,2	5,6±0,3

(пг/мл)			
IL-8 (пг/мл)	22,3±2,3	12±1,2	23,5±1,8
TNF(МЕ/л)	8,2±1,2	5,6±1,6	6,5±1,5

One of the objectives of this scientific study was to determine the significance of cytokines (IL-1, IL-6, IL-8) and the role of tumor necrosis factor-alpha (TNF) in early diagnosis prediction of the course of cardiomyopathy in children. Analysis of the study results showed (Table 5) that the following blood biochemical parameters were elevated in children with DCMP: CFC - 255.9±14.9 ME/L; LDH - 476.9±43.8 ME/L. Blood cytokines were elevated in children with DCMP.

As can be seen from the figure, the most pronounced increase in biochemical markers was observed in children with DCMP, which is confirmed by unfavorable outcomes in the progression of this pathology in children.

Thus, for early diagnosis and prognosis of the course of CMP in children, along with functional examinations, it is necessary to determine cardio specific markers - creatine phosphokinase, lactate dehydrogenase, and immunological indicators - cytokines. The determination of these indicators helps assess the severity of chronic heart insufficiency, predict further development of the disease, and evaluate the effectiveness of therapy.

Reference:
1. Bershova T.V., Bakanov M.I., Basargina E.N., Hasanov A.G. Biochemical markers of cardiac insufficiency development in children with dilated cardiomyopathy // Voprosy Modern Pediatrics. 2015. T. 14. №1. C. 20.
2. Bershova T.V., Bakanov M.I., Basargina E.N., Hasanov A.G. Dynamics of biochemical markers for myocardial remodulation in children with dilated cardiomyopathy in the background of complex therapy // Russian Medical Journal. 2014. №5. C. 25-29.
3. Belokon' N. A. Non-revasive cardiac arrest in children // N. A. Belokon.' - — M., 2009. -210 c.
4. Belova N.R., Basargina E.N., Ivanov A.P., Kupiriyanova O.O. Cardiac rhythm dynamics in treating chronic heart insufficiency in children with dilated cardiomyopathy // Destrophic heart and vessel diseases. 2009. №2. C. 45-54.

5. Maron B.J., Towbin J. A., Thiene G., Antzelevich C. et al. Contemporary definitions and classification of the cardiomyopathies: an American Heart Association Scientific Statement from the Council on Clinical Cardiology, YeartInsufficiency and Transplantation Committee; Quality of Care and Outcomes Reasearch and Functional Genomics and Translational Biology Interdiciplinary Working Groups; and Council on Epidemiologyand Prevention. Circulation 2008; 113: 1807 – 1816. DOI 10.1161/CIRCULATIONAHA.106. 174287.

6. Lipshultz S.E., Cochran T.R., Briston D.A., Brown S.R., et al. Pediatric cardiomyopathies: causes, epidemiology, clinical course, preventive strategies and therapies. Future Cardiol 2013; 9; 817-848. DOI: 10.2217/fca. 13.66.

7. Wilkinson J., Landy D., Colan S., Towbin J., Sleeper L.A., Orav E.J., et al. Pediatric Cardiomyopathy Registry and Heart Insufficiency: Key Results from the First 15 Years. Heart Fail Clin 2010; 6 (4): 401-413. DOI: 10. 1016/ j. hfc. 2010.05.002.

8. Halliday B.P., Cleland J.G., Goldberger J.J., Prasad S.K. Personalizing risk Stratification for Sudden Death in Dilated Cardiomyopthy: The Past, Present, Future. Circulation 2017; 33(9): 888-909. DOI: 10.1161/ CIRCULA-TIONAHA. 116.027.

9. Guidelines for the study of familial dilated cardiomyopathies. Collaborative Research Group of European Human and Capital Mobility Project on Familial Dilated Cardiomyopathy / L. Mestron [et. al.] // Eur. Heart J. – 2000. – Vol. 20. – P. 93-102.

10. Mason J. W. Myocarditis and dilated cardiomyopathy: an inflammatory link / J.W. Mason // Cardiovasc. Res. – 2013. – Vol. 60. - P.5-10.