ISSN 0975-2366
DOI:https://doi.org/10.31838/ijpr/2020.12.04.099

Research Article

Differential diagnostic criteria for dilatational cardiomyopathy and nonreumatic myocarditis in children

DILOROM AKHMEDOVA[1]*, DILFUZA RUZMATOVA[2], NIGORA ALIEVA[3], SAYYORA AKHMEDOVA[4]
[1]Tashkent Pediatric Medical Institute Republic of Uzbekistan
[2,4]Republican Specialized Scientific and Practical Medical Center of Pediatrics of the Ministry of Health of the Republic of Uzbekistan
[3]Tashkent Pediatric Medical Institute Republic of Uzbekistan
*Corresponding Author
Email ID: diloromahmedova@mail.ru, dilfuzaruzmatova87@mail.ru, diloromahmedova@mail.ru, drsayyora@gmail.com
Received: 16.04.20, Revised: 16.05.20, Accepted: 16.06.20

ABSTRACT
Dilatational cardiomyopathy is a severe pathology in childhood, which requires careful study of clinical data and data from functional diagnostics methods (ECG, ECHO) at early stages of detection. This scientific study aimed to determine the clinical, functional features of dilated cardiomyopathy and nonreumatic myocarditis in children. We examined 60 children with DCMP and 40 children with non-reumatic myocarditis aged from 2 months to 18 years, hospitalized in the cardioreumatology department of the Republican Specialized Scientific-Practical Medical Center for Pediatrics of the Ministry of Health of the Republic of Uzbekistan. The control group consisted of 30 practically healthy children.

Keywords: children, cardiomyopathy, echocardiography, radiography, electrocardiography.

INTRODUCTION

According to modern concepts, dilatational cardiomyopathy (DCMP) is defined as a disease of the cardiac muscle of unknown or obscure etiology, characterized by cardiomegaly due to dilatation of heart cavities, especially of the left ventricle (LV), progressive reduction of myocardial contractility, suddenly developing and progressive heart failure, arrhythmic and thromboembolic syndrome, which often ends in sudden death [1]. Dilatation cardiomyopathy is characterized by a continuously progressing course, holds a leading position in the structure of disability and mortality in children, is the main cause of chronic heart failure in childhood [2]. The prevalence of dilated cardiomyopathy varies from 40 cases per 100,000 per year in Europe. It is more common in boys than in girls. The proportion of dilated cardiomyopathy, among other cardiomyopathies, is 60% (8). The rate of sudden death among children with dilated cardiomyopathy ranges from 1.5% to 4%, arrhythmia being the cause of death in most cases. Cardiac 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. In the case of sudden death, ventricular fibrillation has been observed to be high, and a sharp disturbance of pumping function of the left ventricle and an increase in pressure in the cavity contribute to its appearance [4]. Comprehensive introduction of highly informative instrumental methods of cardiac examination, first of all, ehodoppler cardiography, makes it possible to regulate the idea of cardiomyopathy as a nosological unit [3]. According to European experts, the diagnostic criteria of DCMP are [7] left ventricular ejection fraction (LV ejection fraction) less than 45% (according to echocardiography) or fraction shortening of anterior left ventricular size less than 25%. By results of genetic researches of some scientists, in the development of idiopathic DCMP, it has been established that family predisposition, mainly on autosomal-dominant inheritance. Autosomal recessive X-linked and mitochondrial forms of the disease are also found. Acute myocarditis plays a role in the development of DCMP, when first myocardium is affected and then chronic inflammation develops, which in turn leads to remodelling of the heart and its dysfunction (post-inflammatory DCMP) [5,9]. It should be noted that when diagnosing idiopathic DCMP it is necessary to take into account its secondary origin on the background of systemic blood disease, kidney pathology

(uremic cardiomyopathy), on the background of abnormal development of the heart and large vessels (Gerland Blount White syndrome) and inflammatory diseases of the main vessels, mitochondrial diseases, which requires additional methods of research [6,10].The clinical picture of DCMP is variable and determined mainly by the severity of circulatory disorders. The hemodynamic disorder is a consequence of significant reduction of myocardial contractility and cardiac pumping function. First of all, the left ventricle, which is accompanied by an increase in pressure in the heart chambers, their dilatation with subsequent development of stagnation in the small and large circulation circle.Heart Failure Clinic depends on the degree of stagnation in the small and large circulation circle, in the early stages is determined mainly by the signs of left ventricular failure with progressive left ventricular failure (with a clinical picture of pre-edema and pulmonary edema), as the progression of heart disease severity is joined by right ventricular failure (hepatomegaly, oedema syndrome).Considering the severity of clinical symptoms, the progression of clinical manifestations in the dynamics of the disease and the formidable complications that often lead to death, early diagnosis and differential diagnosis of DCMP in children is a crucial problem in clinical pediatrics in general and in pediatric cardiology. Based on the above, this scientific research aimed to determine clinical, functional features of dilatational cardiomyopathy and nonreumatic myocarditis in children.

RESEARCH MATERIALS AND METHODS

We examined 60 children with DCMP and 40 children with non-rheumatic myocarditis aged from 2 months to 18 years who were hospitalized at the cardioreumatology department of the Republican Specialized Scientific-Practical Medical Centre for Pediatrics of the Ministry of Health. The control group consisted of 30 practically healthy children. Analysis of anamnesistical and objective data showed that children's DCMP was 16.6±3.4 months old on average. The diagnosis was made based on complaints, anamnesis data (obstetric history of the mother, history of the child's life and illness, past diseases, nature of the course and duration of the disease) and clinical and functional data (ECG, echocanalysis, Holter ECG monitoring), laboratory (general hematological analysis, biochemical blood analysis with the determination of cardio specific markers - creatine kinase, lactate dehydrogenase) and instrumental (chest X-ray, multispiral computer tomography of the chest) examination methods.

At the time of the examination, the age, sex, height and bodyweight of the child were taken into account. Body surface area (PPT, m2) and body mass index (BMI) were calculated based on body length/height and body weight. The PPT was calculated using the Du Bois formula: PPT = M 0.425 x P 0.725 x 71.84 x 10 -4, where M is body weight (kg), P is body length/height (cm); BMI is calculated using the formula: BMI = M/P2 (kg/m2). ECG was carried out as planned to patients at each hospitalization in cardioreumatology department, both at the primary examination and repeated hospitalization in the department on the Aplio-500 ultrasound device ("Toshiba", Japan) with 3.0-6.5 MHz sector sensors. EchoCG was performed according to standard methods following domestic and foreign guidelines and recommendations. Two-dimensional echocardiography with the determination of echometric indicators was used. Left ventricular myocardial contractility was assessed by the Teicholtz or Simpson ejection fraction (LV) and left ventricular myocardial shortening fraction (LV) [6].

RESULTS AND THEIR DISCUSSION

In children's practice, differential diagnostics of DCMP with other diseases, especially with non-rheumatic carditis, is relevant. The problems of our research were the questions of early diagnostics of DCMP with studying the peculiarities of clinical manifestations and structural-functional state of the cardiovascular system. The study of the clinical course of DCMP and NM showed that both dilatational cardiomyopathy and myocarditis had many similarities in clinical picture and complaints in general.

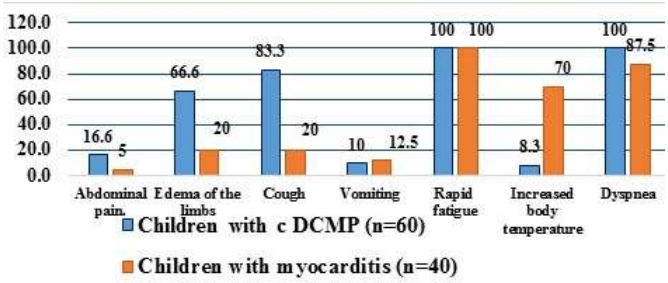


Fig.1: Clinical features of children with DCMP and NM (%)

The occurrence and nature of clinical symptoms were found to depend on the degree of cardiovascular insufficiency. The most typical clinical manifestations for children with DCMP were: rapid fatigue in (100%), swelling of the extremities in (66.6%), shortness of breath in (42%), cough in (83.3%). For children with nonreumatic myocarditis, the more typical clinical manifestations were: increased body temperature (70%), cough (20%), rapid fatigue (100%) (Fig.1). We also assessed hemoglobin levels in children with DCMP and NM. The analysis of the conducted researches has shown, that the average level of hemoglobin in children with DCMP (103,2±1,7 g/l, p<0,01) and with NM (99,4±1,9 g/l, p<0,01) corresponded to anemia of a mild degree and was reliably lower in comparison with indicators of practically healthy children. The average hemoglobin level in children with DEMP and NM did not significantly differ (Table 1).

Table 1: Hemoglobin level assessment

	Almost healthy children n=30	Children with DCMP n=60	Children with NM n=40	P	P_1	P_2
Hemoglobin level (g/l)	121,1±0,45	103,2±1,7	99,4±1,9	<0,01	<0,01	>0.05

Note: P - reliability of differences between indicators of children with practically healthy children and children with DCMP; P_1 - reliability of differences between indicators of children with almost healthy children and children with NM; P_2 - reliability of differences between indicators of children with DCMP and children with NM. The blood electrolyte levels in the children examined were determined for CNS prediction.

Table 2: Blood electrolytes in children with DCMP and NM

Indicators of Electrolytes in blood	Almost healthy children n=30	Children with DCMP n=60	Children with NM n=40	P	P_1	P_2
Potassium (K^+) (3,4-4,7 mmole/l)	4,43±0,09	4,73±0,11	4,27±0,12	<0,05	>0,05	<0,05
Natrium (Na^+) (136-145 mmole/l)	141,68±0,84	135,12±0,97	137,82±0,97	<0,01	>0,05	>0,05
Calcium (Ca^{2+}) (2,25-2,75 mmole/l)	2,25±0,02	1,81±0,04	1,82±0,04	<0,01	<0,01	>0,05

Note: P - reliability of differences between indicators of children with practically healthy children and children with DCMP; P_1 - reliability of differences between indicators of children with almost healthy children and children with NM; P_2 - reliability of differences between indicators of children with DCMP and children with NM.

Analysis of blood electrolytes showed (in Table 2) that children with DCMP, compared to both children with practically healthy children and children with NM, had reliably increased potassium levels (4.73±0.11.p<0.01), and sodium levels were reliably decreased (135.12±0.97.p<0.01), which is typical for congestive heart failure. Calcium level has been reliably reduced at children both with DCMP (1,81±0,04, p<0,01) and with NM (1,82±0,04, p<0,01) concerning indicators of practically healthy children.As is known, one of the most sensitive markers of acute inflammation is C-reactive protein (CRP). To differentiate the genesis of DCMP and NM, a comparative analysis of DRR indicators in children with DCMP and NM was carried out.

Table 3:C-reactive protein parameters in children with DCMP and NM

	Almost healthy children n=30	Children with DCMP n=60	Children with NM n=40	P	P_1	P_2
C-reactive protein (g/l)	2,1±0,4	4,00±0,4	6,0±0,3	<0,05	<0,01	<0,05

Note: P - reliability of differences between indicators of children with practically healthy children and children with DCMP; P_1 - reliability of differences between indicators of children with almost healthy children and children with NM; P_2 - reliability of differences between indicators of

children with DCMP and children with NM. As can be seen from Table 3, the level of C-reactive protein in children with NM (6.0±0.3 g/l) was significantly increased compared to children with DCMP ($p<0.05$) and children with practically healthy children ($p<0.01$). The level of DRR in children with DCMP was also higher than in almost healthy children but to a lesser extent. All patients were diagnosed with heart failure syndrome at the time of examination. In the group of children with DCMP, the CI II B st. (III EF) was detected more often (36,6%), while in the group of children with NM, the highest percentage was registered at CI A I art. (II EF) (37,5%). It is worth mentioning that in the group of children with DCMP, the insufficiency of blood circulation was expressed and the degree of severity was higher than that of children with NM. Thus, children with CI DCMP st. (I EF) did not have it, while in children with NM it was 35,0%. At the same time, the CI III st. (IV EF) was observed in 33,3% of children with DCMP, while in children with NM, this degree was not diagnosed.The X-ray examination revealed an increase in the heart size, mainly due to the left wings, in 66.7% of children with DCMP, while the total expansion was recorded in 13.3% of children, cardiothoracic index being on average 63.3±0.5%. In children with NM, the cardiothoracic index averaged 59.6±0.3%.

The phenomenon of excitement was more frequent in 3 (7.5%) children with NM than in the comparison group (3.3%). The frequency of atrioventricular blockade of different degrees of severity did not differ in the comparison groups. In children with DCMP AV, the siege of 2-3 degrees occurred in 6 (10%) children, while in children with NM no blockade was registered. Violations of ventricular depolarization were observed in the main group more often than in the comparison group 2 (5%), with 6 (10%). Absence or rare cases of extrasystoles were mainly recorded, while frequent extrasystoles were present in single cases. Paired ventricular extrasystoles were found in 5 (8,3%) patients with DCMP and 2 (5%) children with NM. QT interval prolongation was observed in 10% of patients with DCMP, and there were no deviations in the comparison group. Echo CG in children with DCMP and NM revealed: cardiac chamber dilation, systolic dysfunction with reduction of ejection fraction from 40% to 16%, regurgitation on mitral valve and tricuspid valve. Echocardiographic signs in the examined children are presented in Tables 4 and 5.

Table 4: Echocardiographic signs in children with DCMP and NM

Echocardiographic signs	Children with DCMP (n=60) abs. (%)	Children with NM (n=40) abs. (%)
Valve regurgitation (TV and MV)	60 (100%)	20 (50%)
Systolic dysfunction	60 (100%)	40 (100%)
Emission fraction reduction below 40%	60 (100%)	-
Left ventricular wall hypokinesia (LV)	60 (100%)	40 (100%)
Paradoxical movement of the inter ventricular septum (IVS)	20 (33,3%)	-
Hypertrophy with dilatation	5 (8,33%)	-

Studies have shown that in children with DCMP, all echocardiographic disorders prevailed over myocarditis. Thus, all examined children with DCMP showed systolic dysfunction, reduction of ejection fraction below 40%, left ventricular wall hypokinesia, valve regurgitations (MV and TV). Such disorders as systolic dysfunction, reduction of ejection fraction up to 40%, hypokinesia of LV walls in (100%) children with NM were revealed. Paradoxical movements on IVS have observed only in 20 (33.3%) children with DCMP (Table 4).

Table 5: Echocardiographic signs in children with DCMP and CI

Echocardiographic signs	Children with DCMP n=60	Children with NM n=40	Level of reliability P
FDV LV (мл)	108,8±9,04	60,9±4,4	<0,01
FDS LV (мм)	45,70±1,35	39,65±1,2	<0,01
ФВ (%)	31,32±1,64	51,05±0,94	<0,01

Note: P - reliability of differences between comparable groups

As can be seen from Table 5, in children with DCMP, statistically reliable ($p<0.01$) prevailed FDV LV (108.8±9.04 ml) and FDS LV (45.70±1.35 mm). These indicators suggest that

the signs of heart failure were more severe in children with DCMP. The FS was found to be significantly lower in children with DCMP (31.3±1.6%, p<0.01). The results of echocardiographic studies showed that in children with DCMP the finite-diastolic volume of the left ventricle reached from 94 ml to 206 ml, which was associated with an increase in its filling pressure and pronounced dilatation of the left ventricle, which was accompanied with varying degrees of relative insufficiency of mitral in cases and tricuspid valves. According to our data, an increase in the finite-diastolic volume of the left ventricle over 12 mmHg was observed in 40% of children, and systolic and diastolic pressure in the pulmonary artery over 30 and 12 mmHg, respectively. This was accompanied by an increase in right ventricular filling pressure over 6 mmHg. Right ventricular dilatation in 10% of children was accompanied by a dilatation of hollow and hepatic veins, which is typical for stagnation of blood in a large circulation circle. By predominant localization of myocardial lesion by echocardiographic criteria, the children were divided into six variants of DCMP:

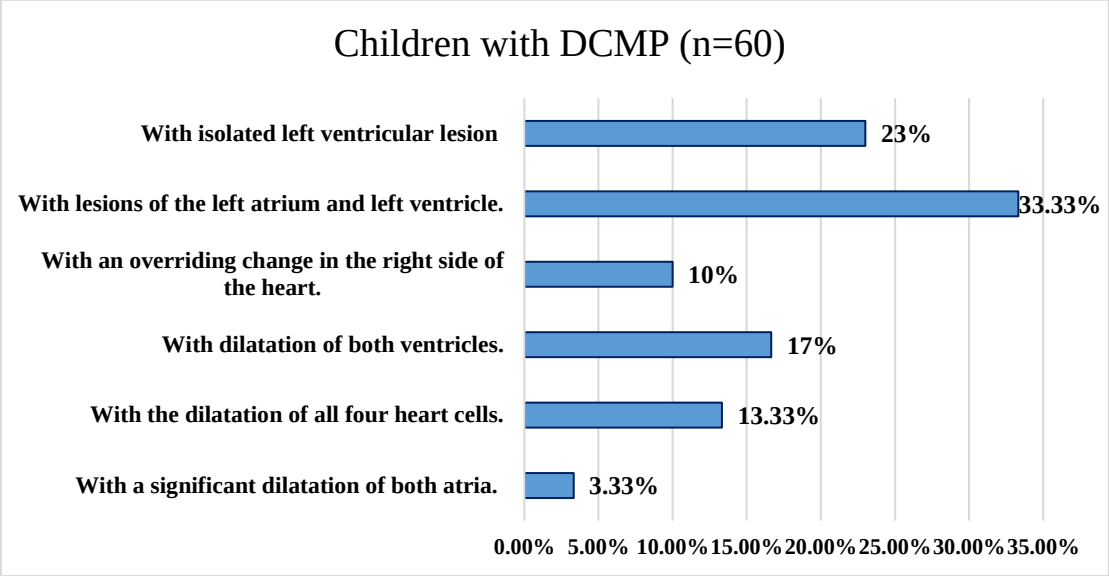
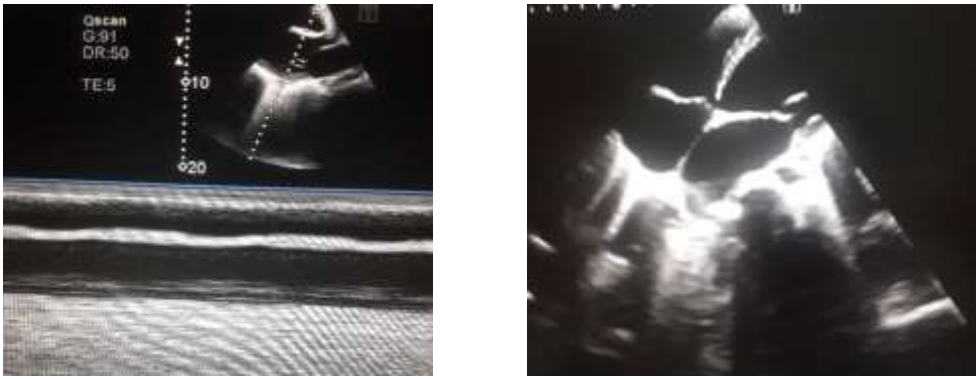


Fig.2: Distribution of children with DCMP according to echocardiographic variants %)

As can be seen from Picture 2, children were subdivided into six variants of DCMP according to echocardiographic criteria by predominant localization of the lesion in myocardium: 14 (23.3%) children with variant 1 - with isolated left ventricular lesion; 20 (33.3%) children with option 2 - with left atrium and left ventricular lesions; 6 (10%) children with variant 3 - with an effective change of right heart regions; 10 (17%) children with the 4th variant - with dilatation of both ventricles; 8 (13,3%) children with the 5th variant - with dilatation of all four heart chambers; 2 (3,3%) children with the 6th variant - with significant dilatation of both atria with minimal changes in the morphofunctional state of the ventricles.In children with the 3rd echocardiographic variant of DCMP, differentiation with arrhythmogenic dysplasia of the right ventricle was made. Among echocardiographic variants 1 and 2 variants (57,1% of children) were the most frequent, which are manifested by left ventricular and left atrial dilatation. In such children, differentiation of DCMP with non-reumatic myocarditis was made. Among them, 23.3% of children had positive dynamics with improvement of functional indices, namely, improvement of myocardial contractility, increase of discharge fraction (up to 45% in dynamics), reduction of FDV LV. In 1 child, the signs of heart failure were eliminated with the restoration of cardiac pumping function (EF 40%, in dynamic 60%). That was the reason for changing the initial diagnosis of DCMP to non-reumatic myocarditis later. In 5 (8.3%) children, a fatal outcome was noted despite the comprehensive therapy as a result of the growing heart failure and arrhythmic syndrome, which is one of the most formidable complications of DCMP. The dilatation of all four heart chambers (5th variant of DCMP) was visualized on the EchoCG in children of this group.



(a) (b)

Fig.3: Echocardiogram b-go A., 2 years. Diagnosis: DCMP: A - total hypokinesia of LV walls; B - dilatation of all heart cells in four-chamber position.

Echocardiographic indices of the 1st and 2nd variants of DCMP are similar to those of acute myocarditis, especially in young children. Distinctive signs in children with DCMP are progressive course of cardiac insufficiency and refractoriness of anti-inflammatory therapy, i.e. progressive reduction of myocardial contractility, lesions and other cardiac chambers to the total expansion of all cardiac chambers.

Thus, the comparative analysis has shown that the development of NM is mainly due to viral etiology and the process is inflammatory. DCMP is characterized by a variety of echocardiographic manifestations, which can be grouped into 6 echocardiographic variants. Distinctive features of both blood electrolyte composition and echocardiographic features in children with DCMP as compared to children with HP are progressive course of heart failure and refractory anti-inflammatory therapy, i.e. progressive reduction of myocardial contractility, lesions and other heart chambers to total expansion of all heart chambers.

To determine the presence of heart failure and assess its severity, much attention is paid to the search for objective criteria, which include the determination of the blood content of cardiac markers. These included creatine phosphokinase (CPK), lactate dehydrogenase (LDH), brain natriuretic peptide (NT-pro BNP), and the de Rhytis AST/ALT ratio, which is normal at 1.5. One of the objectives of this scientific research was to determine the significance of sodiumuretic peptide in early diagnosis and prognosis of chronic heart failure in dilated cardiomyopathy in children, as well as in differential diagnosis with nonreumatic myocarditis.

Table 6: Biochemical marker data in children with DCMP and NM

Biochemical markers	Almost healthy children n=30	Children with DCMP n=60	Children with NM n=40	P	P_1	P_2
Creatinephosphokinae (CPK)	53±4,3	188,7±18	255,9±14,9	<0.01	<0.01	<0,01
Lactate dehydrogenase (LDH) (225-450 ME/l)	175±7.3	476,8±28,9	476,9±43,8	<0.01	<0.01	<0,01
Alaninterransfer (ALT) (<40)	20,03±3,85	31,03±3,8	19,9±1,85	<0,01	<0,01	<0,01
Aspartartaransfer (AST) (<35)	17,5±7.3	50,78±4,7	25,67±2,1	<0,01	<0,01	<0,01
de Ritis AST/ALT ratio (N<1,5)	1,2±0,03	1,9±0,08	1,48±0,09	<0.01	<0.01	<0,01

Note: P - reliability of differences between indicators of children with practically healthy children and children with DCMP; P_1 - reliability of differences between indicators of children with almost healthy children and children with NM; P_2 - reliability of differences between indicators of children with DCMP and children with NM.

The analysis of research results showed (Table 6) that the following blood biochemical parameters were reliably increased in children with nerve

myocarditis: LDH - 255.9±14.9 ME/l (p<0.01); LDH - 476.9±43.8 ME/l (p<0.01); de Ritis AST/ALT ratio - 1.48±0.09 (p<0.01). The expressed increase in all three indicators prevailed in 30% of children with NM, while 53.3% of children with DCMP had an increase more often than one in three biochemical indicators.

The level of sodiumuretic peptide (NT-pro BNP) at all stages of CI was determined to assess the prognosis of heart failure in children with DCMP and NM.

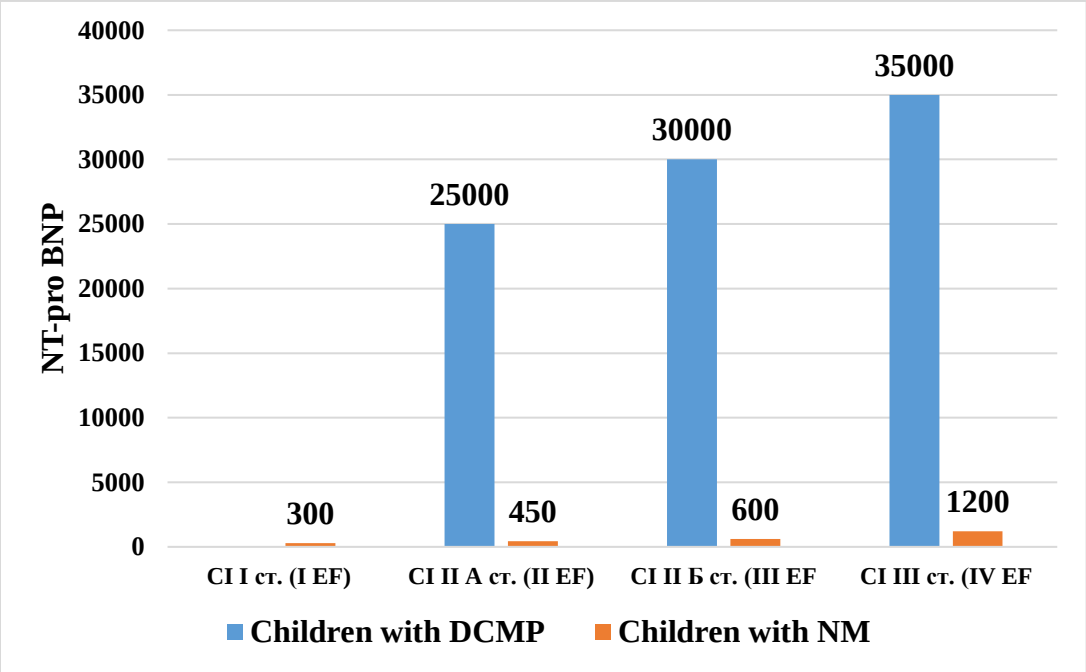


Fig.4: NT-proBNP content in children with DCMP and NM, depending on the CI stage.

The analysis of blood NT-proBNP results showed (pic.4) that children with DCMP were significantly elevated from CI III Art. (IV EF) was up to 38000 pg/ml, while in children with non-reumatic myocarditis with CI III art. (IV EF) was up to 1200 pg/ml (Fig.4).

CONCLUSION

As can be seen, the most expressed increase of biochemical markers is observed at DCMP, which is confirmed by unfavorable outcomes in the process of progression of this pathology in children. All this determines in the presence of risk factors for the development of DCMP, along with functional studies it is necessary to determine cardio specific markers - creatine phosphokinase, lactate dehydrogenase, as well as a brain natriuretic peptide. Determining the level of NT-proBNP in plasma helps to assess the severity of chronic heart failure, to predict further development of the disease, as well as to assess the effectiveness of therapy.

REFERENCES

1. Bershova, T.V.; Bakanov, M.I.; Basargina, E.N.; Hasanov, A.G. Biochemical markers of the cardiac insufficiency development in children with dilatational cardiomyopathy (in Russian) // Voprosy Voprosy Modern'naya pediatriya. 2015. T. 14. №1. p. 20.
2. Bershova, T.V.; Bakanov, M.I.; Basargina, E.N.; Hasanov, A.G. Dynamics of biochemical markers for myocardial remodulation in children with dilatational cardiomyopathy on the background of complex therapy (in Russian) // Russian Medical Journal. 2014. №5. pp. 25-29.
3. Belokonon N.A. Non-reumatic heart rate in children/ N.A. Belokon. - M., 2009. -p.210.
4. Belova, N.R.; Basargina, E.N.; Ivanov, A.P.; Kupiriyanova, O.O. Heart rhythm dynamics in the treatment of chronic heart failure in children with dilatational cardiomyopathy (in Russian). 2009. №2. pp. 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, Yeart Failure 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 Failure: 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.
11. Mohamed Fazze Basha, B., & Mohamed Surputheen, M. (2019). Hybrid feature extraction and firefly based feature selection technique for lung cancer computer aided diagnosis. International Journal of Advanced Science and Technology, 28(13), 587-596. Retrieved from www.scopus.com